CIGARETTE SMOKING AS A RISK FACTOR IN PULMONARY DISEASE

D. M. AVIADO, M.D.

CIGARETTE SMOKING

AS A RISK FACTOR IN PULMONARY DISEASE

Prepared for the Council for Tobacco Research

By

DOMINGO M. AVIADO, M. D.
Professor of Pharmacology
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania 19174

May 17, 1973

Contents (continued)

SUMMARY

1. Introductory remarks. The primary purpose of this review article is to examine the evidence supporting the statement made by the Surgeon General to the effect that "cigarette smoking is the most important cause of chronic obstructive bronchopulmonary disease." The literature that has been examined includes the following: 809 articles on cigarette smoking containing original observations or conclusions; 510 articles on general aspects of pulmonary diseases; and 350 articles which have accepted and publicized the statement of the Surgeon General on the health consequences of smoking. Copies of the total of 1669 articles are being forwarded to the Council for Tobacco Research and are listed in the text as bibliographies of Sections I to VII, publicity bibliographic lists in Section VIII, and additional bibliographic lists in Section X.

II. Occurrence of pulmonary emphysema in nonsmokers. The term chronic obstructive pulmonary disease in the Surgeon General's statement includes pulmonary emphysema. The available evidence does not support the belief that cigarette smoking is the most important cause of pulmonary emphysema. Cigarette smoking is one of the risk factors, which include sex, aging, genetic factors, infection and air pollution. Patients dying of pulmonary emphysema diagnosed by postmortem examination include nonsmokers in a ratio of 22 to 34%. In unselected autopsies, pulmonary emphysema occurs in 10 to 30% of nonsmokers and 50 to 99% of smokers. Patients with antemortem diagnosis of pulmonary emphysema include an incidence of 7.6% who are nonsmokers.

The overall range from 7.6 to 34% of patients with pulmonary emphysema who are nonsmokers is determined by the variable size and nature of the population in the group, with varied sex and genetic factors. The wider range of incidence of smokers (66 to 99%) among patients with pulmonary emphysema does not necessarily mean a cause and effect relationship. Attempts to induce pulmonary emphysema in animals have not been uniformly successful. One widely publicized experiment in the dog shows histopathological signs of emphysema but no functional results. On the other hand, an unpublicized experiment in the rat failed to indicate emphysema on functional and histopathological examination.

III. Chronic bronchitis: concurrence of cigarette smoking, inhalation of pollutants and infection. Chronic bronchitis, clinically diagnosed, occurs in an overall mean of 87% smokers and 13% nonsmokers. Cigarette smoking cannot be identified as the most important risk factor, because it is difficult to exclude air pollution and infection. There is no available model in the laboratory which mimics the pathological and functional features of the human form of chronic bronchitis. The reported experiments pertain to one of several underlying processes in chronic bronchitis, such as mucus secretion, bronchial epithelial changes, nature of the alveolar lining, and the influence of infection. Under specified conditions in animals, exposure to cigarette smoke alters these processes, but this does not necessarily mean that cigarette smoking alone causes chronic bronchitis.

IV. Pulmonary emphysema-bronchitis complex. The mortality statistics which provide the basis for the Surgeon General's statement combine pulmonary emphysema and chronic bronchitis under the term chronic obstructive pulmonary disease. The separate death rates for emphysema and bronchitis are available and should have been handled separately. It appears to the reviewer that combining the two sets of statistics under a single name has improved the results of statistical analysis by establishing the high correlation between cigarette smoking and death rate. The reviewer has not completed a separate analysis of chronic bronchitis and pulmonary emphysema. Nevertheless, the shortcomings of mortality statistics are here listed, including the following: sources of error in filing death certificate, regional differences in air pollution and other factors which influence mortality statistics, factors affecting prognosis of chronic bronchitis and pulmonary emphysema, and inherent characteristics of the individual cigarette smoker.

V. Non-occurrence of chronic pulmonary disease in smokers. The morbidity statistics have been used to support the Surgeon General's statement. The occurrence of coughing and expectoration as derived from answers to a questionnaire does not represent chronic bronchitis or pulmonary emphysema. Some surveys in the United States and in Great Britain and other foreign countries indicate that air pollution, industrial exposure and socio-economic class influence the prevalence of respiratory symptoms.

VI. Bronchopulmonary function in smokers and nonsmokers.

Smokers complaining of respiratory symptoms have low ventilatory function but those who do not complain have normal values. Cigarette smoking causes a transient increase in airway resistance, but the effect on bronchial clearance is variable. These observations do not support the Surgeon General's statement that cigarette smoking causes pulmonary emphysema or chronic bronchitis. A group of smokers with early signs of abnormal ventilatory function need to be kept under surveillance for appearance of either disease. So far, there is no report that chronic bronchitis or pulmonary emphysema has occurred in the course of surveying smokers.

VII. Cardiopulmonary function in smokers and nonsmokers.

The reported difference in ventilation/perfusion ratio, cardiac function, pulmonary circulation and surfactant between smokers and nonsmokers are not completely established. The significance of these differences has not been elucidated.

VIII. Commentary on selected articles and their publicity.

The publications on Smoking and Health appearing in 1964, 1967, 1968, 1969, 1971, 1972 and 1973 have been scrutinized. The Surgeon General's statement that "cigarette smoking is the most important cause of chronic obstructive bronchopulmonary disease" should be revised to read as follows: "Cigarette smoking is one of the risk factors of pulmonary emphysema, chronic bronchitis and other chronic pulmonary disease." The other statements appearing in these publications have similarly been examined and reviewed.

The outcome of the publicity provided by Smoking and Health can be determined by noting editorials, reviews, commentary and resolutions that are appended to this section. Some of them have been selected to illustrate the extent to which the carefully worded statement of the Surgeon General has been understood wrongly to mean that cigarette smoking causes chronic bronchitis and pulmonary emphysema.

IX. Recommendations. It is suggested by the reviewer that scientists, physicians and the general public be informed that cigarette smoking is one of several risk factors, rather than the most important cause of chronic bronchitis and pulmonary emphysema. The nature of investigation of the matter, as undertaken by the epidemiologist, the clinician, the pathologist, and the basic medical scientist, is outlined in this section.

I. INTRODUCTORY REMARKS

That cigarette smoking is one of the important causes of lung diseases in general and of pulmonary emphysema in particular has been accepted by most physicians and the general public. The widespread distribution of the documents on Smoking and Health, prepared by the United States Public Health Service in 1964, 1967, 1968, 1969, 1971, 1972 and 1973, is the most significant factor in this state of affairs. These documents have been regarded as gospels summarizing the evidence that cigarette smoking is the most important of the causes of lung diseases.

There has been no published rebuttal of this statement. On the contrary, the following publications have contributed to the acceptance of the cause and effect relationship between smoking and lung disease: monographs dealing with the subject by the Royal College of Physicians (1962, 1971), Allen et al. (1960), Borgotta and Evans (1968), Diehl (1969), and Hedrick (1969), and review articles by Wallner (1963), Cherniack (1964), Terry (1964), Hay (1967), Horák (1969), Fletcher and Horn (1970), Gilgen and Saigot (1970), Rylander (1970), Rullière (1971), Fréour and Coudray (1971), and Swartz (1971).

The major shortcoming of the evidence presented against cigarette smoking is the conglomeration of reports on specific diseases with non-specific entities. For example, observations on patients diagnosed as having pulmonary emphysema are mixed with mortality statistics derived from death certificates and with morbidity statistics based on symptomatology.

A subject complaining of coughing and shortness of breath, a patient dying with a diagnosis of pulmonary emphysema appearing on the death certificate or with a postmortem diagnosis of pulmonary emphysema, and a patient subjected to functional tests indicating the presence of this disease have been treated in the same manner to arrive at the causation of the disease. This is not proper because of the uncertainty that all these patients indeed have pulmonary emphysema.

The primary purpose of this review article is to examine the scientific evidence that cigarette smoking is the most important of the causes of lung diseases. The articles cited by all the above-mentioned publications and other related ones have been re-examined. The information was classified according to the following factors:

a. Type of lung disease, such as pulmonary emphysema, chronic bronchitis and bronchitis-emphysema complex (also known as chronic obstructive pulmonary disease).

b. Nature of investigation: postmortem examination, antemortem measurement of lung function, morbidity statistics, and mortality statistics.

c. Source of information: normal human subject or patient; state or country of origin; nonsmoker or smoker; male or female; young or old; isolated tissue or intact animal.

d. Other causes of lung disease, such as air pollutants, occupational hazards, genetic factors and infections.

The four items a-d are listed in the order of diminishing importance. The headings and subheadings include the above-listed terms, as well as the following: occurrence, non-occurrence, prevalence and concurrence. They are used to emphasize occurrence, of lung disease in nonsmokers, its non-occurrence in smokers, its prevalence both in smokers and in nonsmokers, and the concurrence of smoking and other risk factors.

BIBLIOGRAPHY

I. INTRODUCTORY REMARKS

Reprint

ALLEN W A, ANGERMANN G, and FACKLER W A: Learning to Live Without Cigarettes, Doubleday & Company, Inc. Garden City pp 1-109, 1968. 1

BORGATTA E F and EVANS R R (editors): Smoking, Health, and Behavior, Aldine Publishing Company, Chicago, pp 52-80, 1968. 2

CHERNIACK L: The respiratory hazards of cigarette smoking. College of General Practice of Canada, Winnipeg, 103-14, 1964. 3

DIEHL H S: Tobacco and Your Health: The Smoking Controversy, McGraw-Hill Book Company, New York, 1-271, 1969. 4

FLETCHER C M and HORN D: Smoking and health. WHO Chron 24:345-70, 1970. 5

FREOUR P and COUDRAY P: Le Tabac. Le tabagisme et ses consequences. Bordeaux Med 4: 2509-82, 1971. 6

GILGEN A: Luftverunreinigung und gesundheit. Zietschrift fur Praventivmedizin 15: 217-30, 1970. 7

HAY D R: An appraisal of the relation of smoking to health NZ Med J 66: 362-69, 1967. 8

HEDRICK J L: Smoking, Tobacco, and Health, Resource Management Corporation, Bethsda, pp 1-48, 1969. 9

HORAK J: Vedecke podklady skodlivosti koureni. Kriticky referat. Scientific evidence on the adverse effect of the smoking habit. Vnitrni lekarstvi 15: 269-82, 1969. 10

ROYAL COLLEGE OF PHYSICIANS: Smoking and health. Pitman Medical London, 1962. 11

ROYAL COLLEGE OF PHYSICIANS: Smoking and Health Now. Pitman Medical and Scientific Publishing Co. Ltd, London. pp 1-148, 1971. 12

RULLIERE R and SAIGOT T: Tabac et poumons. Vie Medicale 52: 3009-17, 1971. 13

RYLANDER R: Djurexperimentella studier av effekter pa andningsorganen. Lakartidningen: 67: 390-96, 1970. 14

SWARTZ H: Tobacco smoke: A noxious air pollutant. Rev Allergy 25:397-405, 1971. 15

TERRY L L: Smoking and health. 538-42 16

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: Smoking and Health. Report of the Advisory Committee to the Surgeon general. pp 1-387, 1964. 17

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: The Health Consequences of smoking 1-227, 1967. 18

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: The health consequences of smoking 1-117, 1968. 19

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: The health consequences of smoking. 1-98, 1969 20

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: The health consequences of smoking. 1-458, 1971 21

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE: The health consequences of smoking. 1973 22

WALLNER L J: Medical aspects of smoking. Trans Am Acad Opthalmol Otolaryngol 281-91, 1963 23

II. OCCURRENCE OF PULMONARY EMPHYSEMA IN NONSMOKERS

If the statement that cigarette smoking is an important cause of pulmonary emphysema is correct, then it would be rare to find nonsmokers who develop this disease. The literature has been examined and the following bibliographic lists are appended:

No. 1. Pulmonary emphysema: etiology and pathogenesis.

No. 2. Pulmonary emphysema: pathological features.

No. 3. Pulmonary emphysema: clinical features.

No. 4. Pulmonary emphysema: therapy.

No. 5. Pulmonary emphysema: alpha$_1$-antitrypsin deficiency.

The articles contained in the above lists relate to emphysema in general and do not report original investigations of its occurrence among nonsmokers and smokers. The information contained in these articles is important to recognize because the emphasis in this section is on pulmonary emphysema rather than cigarette smoking.

The observations concerning the role of smoking in the pathogenesis of pulmonary emphysema, specifically in patients diagnosed clinically and post mortem, are discussed in this section. The experimental attempts to produce emphysema in the animal are reviewed. It is surprising to note at the outset that these attempts have been unsuccessful, with the exception of one which has been widely publicized.

II-A. POSTMORTEM EXAMINATION

In 1819 Laennec first described pulmonary emphysema as a clinical entity characterized by enlargement of air "vesicles" or air spaces. There is some controversy as to the priority of the recognition of the disease since Larson (1964) called attention to a description of gross pathology of emphysematous lung by Matthew Baillie, published in 1803. During the past 25 years there has been confusion in terminology for the lesions characteristic of pulmonary emphysema, chronic bronchitis and asthma. The definition by a committee of the American Thoracic Society has been generally accepted (Harris et al., 1962). The definition is as follows: emphysema is an anatomical alteration of the lung characterized by an abnormal enlargement of the air spaces distal to the terminal nonrespiratory bronchioli, accompanied by destructive changes in the alveolar walls.

Determination of the occurrence of pulmonary emphysema among nonsmokers can be derived from two sets of observations: patients dying of pulmonary emphysema confirmed by histologic examination; postmortem examination in deaths from various causes.

1. Selected patients with pulmonary emphysema. Sweet et al. (1961) reported the first correlation of pathologic patterns with smoking habits in patients dying of pulmonary emphysema in Missouri. Among 194 deaths, the sections from 91 subjects revealed centrilobular lesions specifically ectasia, destruction and departitioning of respiratory

bronchioles. In 78 deaths, panlobular lesions were noted, consisting of progressive and uniform distention of all the terminal ducts and sacs throughout the secondary lobule. The remaining 25 deaths showed combination of centrilobular and panlobular emphysema. The use of tobacco was known in one-fifth of the patients. The results were as follows:

14 Centrilobular cases:	5 nonsmokers,	6 moderate and	3 heavy smokers
19 Panlobular cases:	5 nonsmokers,	3 moderate and	11 heavy smokers
5 Combined cases:	3 nonsmokers,	1 moderate and	1 heavy smoker
38 Total	13	10	15

The above figures indicate that 34% of patients dying of pulmonary emphysema were nonsmokers.

Anderson et al. (1964, 1966) have reported a larger series of 110 patients with known smoking habits dying of pulmonary emphysema. This series, larger than the group reported by Sweet et al., showed a difference in distribution between centrilobular and panlobular lesions, as follows:

83 smokers:	38 panlobular	45 centrilobular
27 nonsmokers:	24 "	3 "
	62	48

Practically all lungs with centrilobular emphysema came from smokers, and panlobular emphysema occurred in random fashion in both smokers and nonsmokers. The incidence of pulmonary emphysema of either type in nonsmokers was 22%.

2. Nonselected patients. Postmortem examination of patients who were not selected for investigation of pulmonary emphysema has been reported by several groups of investigators. Anderson et al. (1970) examined the lungs obtained from 80 nonsmokers in Florida, ranging in age from 37 to 94 years. Twenty-four demonstrated some degree of parenchymal dilatation and disruption which were usually lobular in distribution. Panlobular emphysema of varying severity occurred in 20 patients and centrilobular in 4. The overall incidence of both forms of emphysema was 30% in the group of nonsmokers.

Auerbach et al. (1963, 1966) reported the results of their examination of lung tissue obtained from 1,582 autopsies performed from 1955 through 1960 at a Veterans Administration hospital in New Jersey. The results are expressed in terms of degree of rupture of alveolar septum, fibrosis and thickening of walls of small arteries and arterioles. There was no assessment of degree of panlobular or centrilobular emphysema, so that it is not possible to relate their observations with those of others. They concluded that these pathological changes were highly associated with cigarette smoking and all of them were found to increase with the age of the smoker. Although 120 of 1,340 cases were nonsmokers, it is not possible to state how many of them can be regarded as showing lesions of pulmonary emphysema, similar to those reported by others.

The later report of Auerbach et al. (1972) conformed with the usual practice of specifying if the total pathology of the lung signified emphysema. Between 1963 and 1970, 2,613 men and women who died of the disease were studied at autopsy in seven cooperating hospitals in New Jersey and New York. Their results in males were as follows:

176 nonsmokers	10% pulmonary emphysema	9% no emphysema
181 smoked < 20 cigarettes/day	87% " "	13% " "
658 smoked > 20 cigarettes/day	99.7% " "	0.3% " "

The statistics have been criticized by Panzer (1972). The above results indicate that in unselected autopsy cases 10% of nonsmokers develop pulmonary emphysema. The 87 to 99% incidence of pulmonary emphysema among smokers is the highest ever reported. A 50 to 75% incidence among smokers has been reported by Thurlbeck (1963) from Canada, by Petty et al. (1967) from Colorado, by Ishikawa et al. (1969) from Canada, by Yamanaka (1970) from Japan, by McLaughlin and Tueller (1971) from California, by Otto et al. (1970) in Germany, and by Fingerland et al. (1971) in Czechoslovakia. The statistics for the last-mentioned series are as follows:

145 male nonsmokers	26% pulmonary emphysema	
405 female nonsmokers	30% "	"
109 male ex-smokers	50% "	"
408 male smokers	50% "	"

The series reported from Czechoslovakia show a different incidence of pulmonary emphysema in autopsy of unselected patients from those reported by Auerbach et al. (1972) from the United States. The incidence of emphysema among nonsmokers is 2 to 3 times higher in Czechoslovakia than in the United States, and the incidence of emphysema is half as much in Czechoslovakia.

The series of autopsies performed by Alli (1971) in Nigeria indicate the following:

59 males	25.4% pulmonary emphysema
55 females	12.7% " "
114 total	19.3%

There is a low incidence of smoking among the above cases. The overall incidence of 19% emphysema is midway between the incidence for nonsmokers reported from the United States and Czechoslovakia.

II. OCCURRENCE OF PULMONARY EMPHYSEMA IN NONSMOKERS

A. POSTMORTEM EXAMINATION

Reprint

ALLI A F: Pulmonary emphysema in Ibadan: A pathological study of unselected necropsy lungs. Trop Geogr Med 24: 28-38, 1972. 24

ANDERSON A E Jr, FURLANETO J A and FORAKER A G: Bronchopulmonary ___ derangements in nonsmokers. Am Rev Resp Dis 101: 518-27, 1970. 25

ANDERSON A E Jr, HERNANDEZ J A, ECKERT P and FORAKER A G: Emphysema in lung macrosections correlated with smoking habits. Science 144: 1025-26, 1964. 26

ANDERSON A K Jr, HERNANDEZ J A, HOLMES W L and FORAKER A G: Pulmonary emphysema. Arch Environ Health 12: 569-77, 1966. 27

AUERBACH O, HAMMOND E C, GARFINKEL L and BENANTE C: Relation of smoking and age to emphysema. Whole-Lung section study. N Engl J Med 286: 853-7, 1972. 28

AUERBACH O, STOUT A P, HAMMOND E C and GARFINKEL L: Smoking habits and age in relation to pulmonary changes. Rupture of alveolar septums, fibrosis and thickening of walls of small arteries and arterioles. N Engl J Med 269: 1045-54, 1963. 29

AUERBACH O, STOUT A P, HAMMOND E C and GARFINDEL L: Emphysema and other pulmonary changes in smokers. Histologic evidence. Postgrad Med 40: 95-100, 1966. 30

FINGERLAND A, HUSAK T and BENFLOVA J: Contribution to the investigation of the effect of cigarette smoking. Sb Ved Pr Lek Fak Karlovy Univ 14: 221-34, 1971. 31

HARRIS H W, MENEELY G R, RENZETTI A D Jr, STEELE J D and WYATT J P: Chronic bronchitis, asthma, and pulmonary emphysema. Am Rev Resp Dis 85: 762-68, 1962. 32

ISHIKAWA S, BOWDEN D H, FISHER V and WYATT J P: The "emphysema profile" in two midwestern cities in North America. Arch Environ Health 18: 660-66, 1969. 33

LAENNEC R T H: A Treatise on Diseases of the Chest. History of Medicine Series No. 17 - N Y Acad Med; Hafner, 1819 (reprinted 1962) pp 81 -97. 34

LARSON R K: Historical note on emphysema. Am Rev Resp Dis 91: 277-78, 1965. 35

McLAUGHLIN R F and TUELLER E E: Anatomic and histologic changes of early emphysema. Chest 59: 592-99, 1971. 36

OTTO H, ZEILHOFER R and REISSINGER O: Vergleichende untersuchungen zur klinik und symptomatik morphologisch gesicherter emphysemfalle. (Clinical signs of histologically proven emphysema). 776-85, 1970. 37

PANZER F: Emphysema and smoking: additional data. N Engl J Med 286: 1321, 1972. 38

PETTY T L, RYAN S F and MITCHELL R S: Cigarette smoking and the lungs. Arch Environ Health 14: 172-77, 1967. 39

Bibliography II-A

Reprint

SWEET H C, WYATT J P, FRITSCH A J and KINSELLA P W: Panlobular and centrilobular emphysema. Correlation of clinical findings with pathologic patterns. Ann Intern Med 55: 565-81, 1961. 40

THURLBECK W M: A clinico-pathological study of emphysema in an American hospital. Thorax 18: 59-67, 1963. 41

YAMANAKA A: Pulmonary emphysema in Japan. Pathol Microbiol 35: 161-6, 1970. 42

II-B. ANTEMORTEM STUDIES

The extent of the occurrence of pulmonary emphysema among nonsmokers can be derived from a review of groups of patients with a diagnosis of pulmonary emphysema based on clinical studies. The reports are as follows:

Abbott et al. (1953)	250 males and females from Georgia:	41 nonsmokers
Mitchell (1962) Mitchell et al. (1964)	123 males and females from Colorado:	8 nonsmokers
Kahana et al. (1963)	19 males from Canada:	1 nonsmoker
Seebohm and Bedell (1963)	10 males from Iowa:	0 nonsmoker
Antonio (1963)	16 males or females from Philippines:	4 nonsmokers
Boushy and Lewis (1964)	61 males and females from Michigan:	4 nonsmokers
Ray (1965)	360 males and females from Virginia:	8 nonsmokers
Burgess and Burgess (1966)	204 males and females from Rhode Island:	15 nonsmokers
Boushy et al. (1968)	49 males from Louisiana:	0 nonsmoker
Lépine and Myre (1969)	41 males or females from Canada:	0 nonsmoker
Saha and Jain (1970)	50 males and females from India:	8 nonsmokers

The above reports are based on series numbering 10 to 360 patients with clinical diagnosis of pulmonary emphysema. In the total number of 1,183 selected patients, there are 89 nonsmokers. The incidence of 7.6% of nonsmokers among patients with pulmonary emphysema is lower than that based on postmortem examination (see Section II-A.)

Patients suffering from pulmonary emphysema have been investigated while inhaling cigarette smoke. The results have so far been conflicting. Bickerman and Barach (1954) compared the response of 91 patients suffering from chronic nontuberculous pulmonary disease, most of them having pulmonary emphysema, with that of 27 healthy subjects. The smoking of 3 cigarettes did not increase bronchospasm or impair ventilatory function. There was a reduction of vital capacity and of maximal breathing capacity in 10 patients who had bronchial asthma. Both measurements were increased in 10 patients with emphysema, in whom coughing provoked by smoking resulted in expectoration.

The observations of Eich et al. (1956, 1957) were made on 15 patients with pulmonary emphysema. After the smoking of one cigarette, there was an increase in airway resistance in 14 of them and no significant change in pulmonary compliance.

The above-cited observations do not necessarily imply that cigarette smoking leads to pulmonary emphysema. There are numerous data relating to the effects of cigarette smoking on lung function of healthy subjects that are discussed in Section VI.

BIBLIOGRAPHY

II. OCCURRENCE OF PULMONARY EMPHYSEMA IN NONSMOKERS

B. ANTEMORTEM STUDIES

Reprint

ABBOTT O A, HOPKINS W A, VAN FLEIT and ROBINSON J S: A new approach to pulmonary emphysema. Thorax 8: 116-132, 1953. 43

ANTONIO R N: Diffuse obstructive emphysema -- clinico-physiological manifestations among Filipinos. Bull Quezon Inst 7: 127-39, 1963. 44

BICKERMAN H A and BARACH A L: The effect of cigarette smoking on ventilatory function in patients with bronchial asthma and obstructive pulmonary emphysema. J Lab Clin Med 43: 455-62, 1954. 45

BOUSHY S F and LEWIS B M: The natural history of emphysema. Geriatrics 19: 910-19, 1964. 46

BOUSHY S F, KOHEN R, BILLIG D M and HEIMAN M J: Bullous emphysema: clinical, roentgenologic and physiologic study of 49 patients. Dis Chest 54: 327-34, 1968. 47

BURGESS A M and BURGESS S B: Chronic obstructive pulmonary emphysema. A review, with special reference to its relation to cigarette smoking. R I Med J 49: 461-5, 1966. 48

EICH R H, GILBERT R and AUCHINCLOSS J H Jr: Effects of smoking on respiratory mechanics in chronic pulmonary emphysema. Clin Res Proc 4: 151-52, 1956. 49

EICH R H, GILBERT R and AUCHINCLOSS J H Jr: The acute effects of smoking on the mechanics of respiration in chronic obstructive pulmonary emphysema. Am Rev Tuberc 76: 22-32, 1957. 50

KAHANA L M, ARONOVITCH M and PLACE R: A comparative study of the clinical and functional pattern in emphysematous patients with and without chronic respiratory failure. Am Rev Resp Dis 87: 699-716, 1963. 51

LEPINE C and MYRE M: L'emphyseme pulmonaire. Confrontations cliniques et physiologiques avec une reference speciale a l'usage de la cigarette. Union Med Can 98: 1853-58, 1969. 52

MITCHELL R S: Diffuse pulmonary emphysema and occupation. JAMA 181: 71-77, 1962. 53

MITCHELL R S, VINCENT T N and FILLEY G F: Cigarette smoking chronic bronchitis, and emphysema. JAMA 188: 12-16, 1964. 54

RAY E S: Pulmonary emphysema. A disease of cigaret smokers. Virginia Med Monthly 92: 170-73, 1965. 55

SAHA N C and JAIN S K: Chronic obstructive lung disease in Delhi. A comparative study. Indian J Chest Dis 12: 40-51, 1970. 56

SEEBOHM P M and BEDELL G N: Primary pulmonary emphysema in young adults. Am Rev Resp Dis 87: 41-46, 1963. 57

II-C. RISK FACTORS IN THE PATHOGENESIS OF PULMONARY EMPHYSEMA

That pulmonary emphysema may occur in nonsmokers can only be interpreted to mean that smoking is not the only important causative factor. There are five other factors that are as significant as cigarette smoking, namely: sex, age, genetic factors, infection, and air pollution. They can properly be described as risk factors which predispose a subject to the development of pulmonary emphysema. The first three are discussed in this section but the last two are dealt with in Section III because they contribute to the pathogenesis of chronic bronchitis as well as of pulmonary emphysema.

1. Sex and pulmonary emphysema. It has generally been accepted that pulmonary emphysema occurs predominantly in males. The routine postmortem examination shows the following incidence of the disease for male in relation to female subjects:-- 2:1 as determined by Smith (1965), 3:2 by Azcuy et al. (1962), and 1:1 by Snider et al. (1962). The emphysema registries show a higher ratio of 9:1 reported by Mitchell and Filley (1964), Burrows et al. (1965), and Webster et al. (1968). There were no differences in laboratory data and family history between males and females.

The smoking habits of females are discussed in three additional reports. Bedell and Seebohm (1960) described a group of 12 women with pulmonary edema, ranging in age from 31 to 65 years, two of whom were nonsmokers. Lindall et al. (1967) evaluated pulmonary function in 101 females without lung disease. The women smokers were found to have lower mid-maximal flow rates and ratios of forced expiratory volume to

vital capacity, compared with nonsmokers. Carilli et al. (1973) reviewed chest films of 92 women and could note changes such as diffuse linear and nodular fibrosis in smokers that were not seen in nonsmokers. These observations are similar to those reported by others in males and do not detract from the original premise that there is a higher incidence of pulmonary emphysema in males. Anderson et al. (1972) reviewed a series of necropsy cases and concluded that sex has an effect on the incidence of emphysema over and above the difference between the sexes in the amount of smoking.

2. Aging and pulmonary emphysema. The high incidence of pulmonary emphysema in the aged has been discussed in a monograph (Gross, , 1964) and several review articles (Burrows, 1962; Cander and Blumenthal, 1963; Alvarez, 1964; Herberg, 1966; Niesenbaum, 1968). The mechanism by which aging leads to emphysema has not been identified. Degeneration and loss of elasticity occur, which are terms of a descriptive nature and do not explain how the aging operates as a risk factor.

3. Genetic factors. Pulmonary emphysema appears in white males more frequently than in the Negro. The relative incidence varies, depending on the manner of comparison. Counting of clinical cases reveals that the incidence in white males is 3 or 4 times more frequent than in Negro males (Murphy et al., 1962). Deaths from emphysema in white males are 10 times more frequent (Ray, 1965). The lower incidence in the Negro does not relate to dissimilar smoking habits or a different

effect of smoking upon maximal terminal flow (Canter and Luchsinger, 1967, 1968). The Negro male has smaller vital capacity, which would not account for a lower incidence of pulmonary emphysema (Damon, 1966). The East Indians residing in Jamaica are reported to suffer more from the centrilobular type of pulmonary emphysema than the Chinese, Negro and white residents (Hayes and Summerell, 1969; Hayes, 1970).

A genetic defect has been identified in some patients with pulmonary emphysema. A deficiency in alpha-antitrypsin can be inherited and is believed to participate in the pathogenesis of pulmonary emphysema (see monograph by Eriksson, 1965, review article by Guenter et al., 1971 and bibliographic list no. 5). Patients have been reported to have pulmonary emphysema and alpha-antitrypsin deficiency who were nonsmokers: 2 out of 9 in Massachusetts (Talamo et al., 1968), 1 out of 8 in Washington (Bell, 1970), 1 out of 12 in England (Jones and Thomas, 1971), 1 out of 6 in Texas (Stevens et al., 1971), 3 out of 10 in Minnesota (Black et al., 1972). It has been proposed that cigarette smoking provokes the early onset of emphysema in subjects with this genetic defect (Levine et al., 1970; Mittman et al., 1971 a, b; Fallat et al., 1971, 1973; Fallat, 1972; Hutchison et al., 1971, 1972). However, the evidence is not unequivocal and is based on the coexistence of emphysema and deficiency of alpha-antitrypsin among smokers. Observations have been made which suggested that smoking caused emphysema in deficient subjects. There is no association between prevalence of pulmonary

disease, incidence of antitrypsin deficiency and smoking habits (Geisler et al., 1972; Sano et al., 1972). Furthermore, some subjects with this genetic defect, who are smokers, do not show signs of pulmonary emphysema (Eriksson, 1965).

The identification of alpha-antitrypsin deficiency as a genetic defect in some patients with pulmonary emphysema raises the possibility of other defects which have not yet been identified (see review articles by Gedda, 1967, McKusick and Mutalik, 1968, and Larson et al., 1970). Patients with emphysema have been characterized by personality features (De Cencio et al., 1968), somatotype (Damon, 1961; Damon et al., 1962), baldness (Buechner et al., 1964), and longevity (Deutscher and Higgins, 1970). There are personality features which are inherited by the individual (Heath, 1958; De Cencio et al., 1968; Clark and Cochrane, 1970; Ochsner and Damrau, 1970).

BIBLIOGRAPHY

II. OCCURRENCE OF PULMONARY EMPHYSEMA IN NONSMOKERS

C. RISK FACTORS IN THE PATHOGENESIS OF PULMONARY EMPHYSEMA

ALVAREZ W C: Is emphysema a geriatric disease? Geriatrics 19: 139-42, 1964. Reprint 58

ANDERSON J A, DUNNILL M S and RYDER R C: Dependence of the incidence of emphysema on smoking history, age, and sex. Thorax 27: 547-51, 1972. 59

BEDELL G N and SEEBOHM P M: Primary pulmonary emphysema in women. J Iowa Med Soc 56: 258-62, 1966. 60

BELL R: The radiographic manifestations of alpha-1 antitrypsin deficiency. An important recognizable pattern of chronic obstructive pulmonary disease (COPD). Radiology 95: 19-24, 1970. 61

BLACK L F, HYATT R E and STUBBS S E: Mechanism of expiratory airflow limitation in chronic obstructive pulmonary disease associated with α_1 antitrypsin deficiency. Am Rev Resp Dis 105: 891-99, 1972. 62

BUECHNER H A, BROWN M and TRETOLA R J: Baldness and emphysema. J Louisiana Med Soc 116: 329-32, 1964. 63

BURROWS B: Pulmonary and respiratory diseases in the aged. Postgrad Med 31: 296-302, 1962. 64

CANDER L and BLUMENTHAL W S: Emphysema and the aging lung. Geriatrics 18: 413-420, 1963. 65

CANTER H G and LUCHSINGER P C: Interrelationships of smoking habits, race and maximal terminal flow. Am Rev Resp Dis 96: 147-48, 1967. 66

CANTER H G and LUCHSINGER P C: Interrelationships of smoking habits, race and maximal terminal flow. Am Rev Resp Dis 97: 1071-75, 1968. 67

CARILLI A D, KOTZEN L M and FISCHER M J: The chest roentgenogram in smoking females. Am Rev Resp Dis 107: 133-36, 1973. 68

CLARK T J H and COCHRANE G M: Effect of personality on alveolar ventilation in patients with chronic airways obstruction. Br Med J 273-75, 1970. 69

GEDDA L: Il chronon, ossia la dimensione tempo dell'unita ereditaria. Gazz Sanit 38: 323-26, 1967. 70

DAMON A: Constitution and smoking. Science 134: 339-41, 1961. 71

DAMON A: Constitution and smoking in Italian-American factory workers. Am J Phys Anthropol 20: 67-68, 1962. 72

DAMON A: Negro-white differences in pulmonary function (Vital capacity, timed vital capacity, and expiratory flow rate). Human Biol 38: 380-93, 1966. 73

DeCENCIO D V, LESHNER M and LESHNER B: Personality characteristics of patients with chronic obstructive pulmonary emphysema. Arch Phys Med Rehabil 49: 471-75, 1968. 74

DEUTSCHER S and HIGGINS M W: The relationship of parental longevity to ventilatory function and prevalence of chronic nonspecific respiratory disease among sons. Am Rev Resp Dis 102: 180-89, 1970. 75

ERIKSSON S: Studies in alpha-antitrypsin deficiency. Acta Medica Scandinavica 177 (Supplementum 432): 1 -85, 1965. 76

FALLAT R J: To the Editor. Ann Intern Med 72: 438-39, 1970. 77

FALLAT R J, POWELL M R, KUEPPERS F and LILKER E: ^{133}Xe ventilatory studies in 1-antitrypsin deficiency. J Nucl Med 14: 5-13, 1973. 78

FALLAT R , POWELL M, KUEPPERS F, NADEL J and MURRAY J: Chronic obstructive pulmonary disease with intermediate alpha$_1$-antitrypsin deficiency. Chest 59: (Suppl 5) 205-225, 1971. 79

GEISLER L S, BACHMANN G W, LAUMEN F, NOLTE D, WENTZEL H and ROST H-D: α_1-antitrypsin und immunglobuline bei chronisch unspezifischen lungenerkrankuggen und lungentuberkerkulose. Dtsch Med Wochenschr 97: 329-35, 1972. 80

GROSS P: Environmental stress and the aging lung. The pulmonary effects of air pollution. In: Aging of the lung. Perspectives. The tenth Hahnemann Symposium. Edited by Leon Cander. Grune & Stratton, New York. pp. 217-26, 1964. 81

GUENTER C A, WELCH M H and HAMMARSTEN J F: Alpha anititrypsin deficiency and pulmonary emphysema. Ann Rev Med 22: 283-92, 1971. 82

HAYES J A and SUMMERELL J M: Emphysema in a non-industrialized tropical island. Thorax 24: 623-25, 1969. 83

HAYES J A: Racial, occupational, and environmental factors in relation to emphysema in Jamaica. Chest 57: 136-40, 1970. 84

HEATH C W: Differences between smokers and nonsmokers. Arch Intern Med 101: 377-88, 1958. 85

HERBERG D: Seniles und obstruktives emphysem. Diagnose, atiologic und begutachtung. Beitr Klin Tuberk 133: 75-91, 1966. 86

HUTCHISON D C S, BARTER C E, COOK P J L, LAWS J W, MARTELLI N A and HUGH-JONES P: Severe pulmonary emphysema. A comparison of patients with and without α_1-antitrypsin deficiency. Q J Med 41: 301-15, 1972. 87

HUTCHISON D C S, COOK P J L, BARTER C E, HARRIS H and HUGH-JONES P: Pulmonary emphysema and α_1-antitrypsin deficiency. Br Med J 1: 689-94, 1971. 88

JONES M C and THOMAS G O: Alpha, antitrypsin deficiency and pulmonary emphysema. Thorax 26: 652-62, 1971. 89

LARSON R K, BARMAN M L, KUEPPERS F and FUDENBERG HH: Genetic and environmental determinants of chronic obstructive pulmonary disease. Ann Intern Med 72: 627-32, 1970. 90

LEVINE B W, TALAMO R C, SHANNON D C and KAZEMI H: Alteration in distribution of pulmonary blood flow. An early manifestation of Alpha$_1$ antitrypsin deficiency. Ann Intern Med 73: 397-401, 1970. 91

LINDALL A, MEDINA A, GREIMER J T: A reevaluation of normal pulmonary function measurements in the adult female. Am Rev Resp Dis 95: 1061-1064, 1967. 92

McKUSICK V A and MUTALIK G S: Genetics and pulmonary disease. In: The Lung. Edited by A A Liebow and D E Smith. The Williams and Wilkins Company, Baltimore, 1968. PP. 187-202. 93

MITTMAN C, LIEBERMAN J, MARASSO F and MIRANDA A: Smoking and chronic obstructive lung disease in alpha$_1$-antitrypsin deficiency. Chest 60: 214-221. 1971A. 94

MITTMAN C, LIEBERMAN J, MARASSO F and MIRANDA A: Pulmonary alveolar proteinosis and blood dyscrasias. Clin Res 19: 146, 1971B. 95

MURPHY R E, KATZ S, MASSARO D J and LUCHSINGER P C: Is emphysema a disease predominantly of the while male? JAMA 181: 726-27: 1962. 96

NIESENBAUM L: Problems of pulmonary disease in the aged. Geriatrics 23: 127-31, 1968. 97

OCHSNER A and DAMRAU F: Control of cigarette habit by psychological aversive conditioning: Clinical evaluation in 53 smokers. J Am Geriatr Soc 18: 365-69, 1970. 98

RAY E S: Relative incidence of pulmonary emphysema among negroes and whites of both sexes. Med Coll Virginia Quart 1: 50-51, 1965. 99

SANO T, , YODOYAMA M and RHOADS G G: Clinical significance of α_1-antitrypsin level -- a preliminary evaluation among Japanese men. Hawaii Med J 31: 27-32, 1972. 100

STEVENS P M, HNILICA V S, JOHNSON P C and BELL R L: Pathophysiology of hereditary emphysema. Ann Intern Med 74: 672-80, 1971. 101

TALAMO R C, ALLEN J D, KAHAN M G and AUSTEN F: Hereditary alpha$_1$-antitrypsin deficiency. N Engl J Med, 278: 345-51, 1968. 102

WEBSTER J R Jr, KETTEL L J, MORAN F, BUGAIESKI S and CUGELL D W: Chronic obstructive pulmonary disease. A comparison between men and women. Am Rev Resp Dis 98: 1021-26, 1968. 103

AZCUY A D, ANDERSON A E, and FORAKER A E: The morphological spectrum of aging and emphysematous lungs. Ann Intern Med 51:1, 1962. 103a

BURROWS B, NIDEN A H, BARCLAY W R and KASIK J H: Chronic obstructive lung disease: I. Clinical and physiologic findings in 175 patients and their relationship to age and sex. Amer Rev Resp Dis 91:521, 1965. 103b

MITCHELL R S and FILLEY G F: Chronic obstructive bronchopulmonary disease: I. Clinical features. Amer Rev Resp Dis 89:360, 1964. 103c

SMITH V K: Survey of types and severity of emphysema in routine autopsies. Aust Ann Med 14:28, 1965. 103d

SNIDER G L, BRODY J S and DOCTOR L: Subclinical pulmonary emphysema. Amer Rev Resp Dis 85:666, 1962. 103e

II-D. EXPERIMENTAL PULMONARY EMPHYSEMA

The publicity surrounding the experimental induction of pulmonary emphysema by Auerbach and his collaborators has given the impression that the problem has been settled. Numerous attempts to study the matter have been made by others and the results have been negative, which have not been publicized. There is still considerable doubt that cigarette smoking can lead to pulmonary emphysema in experimental animals. The problems in induction of emphysema have been discussed by Strawbridge (1960a), Thurlbeck (1963), Boren (1965), Reif et al (1970) and Mittman (1972).

1. Experiments in the dog. Two groups of dogs have been exposed to cigarette smoke through a tracheostomy tube by Auerbach and his collaborators: ten dogs for 420 days (Auerbach, 1967, 1969; Auerbach et al., 1967, 1968, 1970; Cahan and Kirman, 1968) and 97 dogs up to 876 days (Hammond et al., 1970; Frasca et al., 1971). The results are entirely histopathological in nature, which the investigators have interpreted to indicate pulmonary emphysema. Their interpretation has been criticized by other histopathologists and nothing can be added to this controversy (see Section III). One criticism that has been entirely ignored is the lack of measurements of lung function, which other investigators have developed for application to the dog and other animal species.

Anderson et al. (1964) and Hernandez et al. (1966) exposed greyhounds to hyperinflation of the lung or cigarette smoke. Lungs from

control animals demonstrated significant amounts of naturally occurring disease. The lungs from animals exposed to cigarette smoke showed lesions that were inflammatory in nature. Although there was parenchymal disruption, the pattern of smoke exposure employed with the dog is so different from the habit in man that the authors could not readily transfer their conclusion to apply to the human form of emphysema. Rockey and Speer (1966) and Syzganov et al. (1971) made similar observations and conclusions in the dog. The results of applying a smoking machine in dogs, which simulate those of human inhalation, have not been reported (Bair et al., 1969). Marco et al. (1971) and Mass et al. (1972) induced experimental emphysema in dogs, using leukocyte homogenate. Their findings are entirely histological in nature.

2. Experiments in the rat. Both histological and physiological techniques have been applied to the rat lung to demonstrate conclusively that pulmonary emphysema has developed. The model consists of a combination of tracheal ligation and intratracheal injection of papain. After 4 to 6 weeks, there is an increase of functional residual capacity and the lung shows histological signs of emphysema (Palecek et al., 1967). Concurrent administration of progestational agents retards the development of emphysema (Ito and Aviado, 1968a; Aviado and McKinney, 1969; Aviado and Carrillo, 1969; Shore and Aviado, 1969; Inoh and Aviado, 1971). The concurrent administration of cigarette smoke does not influence the emphysematous

process (Ito and Aviado, 1968b; Aviado et al., 1970). Inhalation of cigarette smoke daily for 8 weeks does not increase functional residual capacity. In these rats exposed to cigarette smoke, there is an increase in pulmonary resistance, which is discussed further in another section relating to the airways.

The inhalation of nitrogen dioxide in the rat causes the development of pulmonary emphysema (Freeman and Haydon, 1964; Haydon et al, 1965; Freeman, 1968; Freeman et al., 1968 a, b, c; 1969). The concentration necessary to induce the lesions is approximately 1,000 times the amount of nitrogen dioxide present in cigarette smoke (Haagen-Smit et al., 1959; Bokhoven and Niessen, 1961). The phenomenon is of toxicological interest when nitrogen dioxide is present as a pollutant or a chemical fume that is inhaled (von Oettingen, 1941; Lowry and Schuman, 1956; Becklake et al., 1957; Gray, 1959). In this context, nitrogen dioxide has the following effects in rats and other animal species: reduced resistance to bacterial pneumonia (Ehrlich and Henry, 1968; Henry et al., 1969, 1970), alteration in collagen fibrils and basement membranes of the lung (Stephens et al., 1971); increase in metabolic activity of lung tissue (Buckley and Loosli, 1969); increase in nonelastic resistance of the lung (Haydon et al., 1967); and increase in lung tissue antibody in the blood (Balchum et al., 1965; Boren et al., 1965). Gross et al. (1968 a, b) did not observe any acceleration by nitrogen oxide of experimental silicosis caused by coal or blast furnace stack dust in rats.

Cadmium is another constituent of cigarette smoke (Nandi et al., 1969). Exposure to cadmium fumes causes lesions in the human lung similar to those of emphysema (Bonnell, 1955; Bonnell et al., 1959; Smith et al., 1960). However, the phenomenon has not been examined in rats or other animal species to determine whether the amount of cadmium in cigarette smoke is sufficient to produce pulmonary lesions.

3. Experiments in other animal species. Experimental emphysema in several animal species has been reported but not the influence of cigarette smoke. The following species have been used: hamster (Goldring et al., 1968; Gross and de Treville, 1969), rabbit (Strawbridge, 1960 B and C; Boatman and Martin, 1965), piglet (Glauser and Glauser, 1969); horse (Gillespie et al., 1964, 1966; Gillespie and Tyler, 1967; Eberly et al., 1966; McLaughlin et al., 1965), and cow (Carlson et al., 1968; Carlson et al., 1972).

II. OCCURRENCE OF PULMONARY EMPHYSEMA IN NONSMOKERS

D. EXPERIMENTAL PULMONARY EMPHYSEMA

Reprint

ANDERSON A E,Jr, AZCUY A, BATCHELDER T L and FORAKER A G: Experimental analysis in dogs of the relationship between pulmonary emphysema, alveolitis, and hyperinflation. Thorax 19: 420-32, 1964. 104

AUERBACH O: Pathological findings in lungs of dogs following exposure to cigarette smoke. In: Transactions of the 26th VA armed forces pulmonary disease research conference. Prepared and edited by VA department of medicine and surgery, 1967, p. 33. 105

AUERBACH O: Emphysema: Human and experimental. In: Conference on inhalation carcinogenesis. Sponsored by National Cancer Institute and U.S. Atomic Energy Commission, 1969, p. 20. 106

AUERBACH O, HAMMOND E C, KIRMAN D and GARFINKEL L: Emphysema produced in dogs by cigarette smoking. JAMA 149: 241-46, 1967. 107

AUERBACH O, HAMMOND E C, KIRMAN D and GARFINKEL L: Emphysema produced in dogs by cigarette smoking. In: Inhalation carcinogenesis Edited by M G Hanna Jr, P Nettersheim, and J R Gilbert. U.S. Atomic Energy Commission (Division of technical information) Information Interscience Incorporated, 1970, pp. 375-87. 108

AUERBACH O, HAMMOND E C, KIRMAN D, GARFINKEL L and STOUT A P: The effect of direct cigarette smoke inhalation on the respiratory tree of dogs. Nat Cancer Inst Monogr 28: 65-77, 1968. 109

AVIADO D M and CARRILLO L R: Hormones and pulmonary effects of tobacco. I. Corticosteroids and their antiasthmatic action. Arch Environ Health 18: 925-933, 1969. 110

AVIADO D M and McKINNEY G R: Oral progestagens and experimental pulmonary emphysema. Pharmacol Res Comm 1: 283-87, 1969. 111

AVIADO D M, SADAVONGVIVAD C and CARRILLO L R: Cigarette smoke and pulmonary emphysema. Influence of bronchodilators and biogenic amines in experimental induction in rats. Arch Environ Health 20: 483-87, 1970. 112

BAIR W J, PORTER N S, BROWN D P and WEHNER A P: Apparatus for direct inhalation of cigarette smoke by dogs. J Appl Physiol 26: 847-50, 1969. 113

BALCHUM O J, BUCKLEY R D, SHERWIN R and GARDNER M: Nitrogen dioxide inhalation and lung antibodies. Arch Environ Health 10: 274-77, 1965. 114

BECKLAKE M R, GOLDMAN H I BOSMAN A R and FREED C C: The long-term effects of exposure to nitrous fumes. Am Rev Tuberc 76: 398-409, 1957. 115

BLAIR W H, HENRY M C and EHRLICH R: Chronic toxicity of nitrogen dioxide. II. Effect on histopathology of lung tissue. Arch Environ Health 18: 186-92, 1969. 116

BOATMAN E S and MARTIN H B: Electron microscopy in pulmonary emphysema of rabbits. Am Rev Resp Dis 91: 197-205, 1965. 117

BOKHOVEN C and NIESSEN H J: Amounts of oxides of nitrogen and carbon monoxide in cigarette smoke, with and without inhalation. Nature 192: 458-59, 1961. 118

BONNELL J A: Emphysema and proteinuria in man casting copper-cadmium alloys.

Bibliography II-D

Reprint

BONNELL J A, KAZANTZIS G and KING E: A follow-up study of men exposed to cadmium oxide fume. Br J Ind Med 16: 135-47, 1959. 120

BOREN H G: Environmental emphysema. Am Rev Resp Dis 92: 1-15, 1965. 121

BOREN H G, DELAHANT A B and STEENKEN W: Reactions of guinea pig lung to injected lung homogenates. Medicina Thoracalis 22: 355-64, 1965. 122

BUCKLEY R D and LOOSLI C G: Effects of nitrogen dioxide inhalation on germfree mouse lung. Arch Environ Health 18: 588-95, 1969. 123

CAHAN W G and KIRMAN D: An effective system and procedure for cigarette smoking by dogs. J Surg Res 8: 567-75, 1968. 124

CARLSON J R, DYER I A and JOHNSON R J: Tryptophan-induced interstital pulmonary emphysema in cattle. Am J Vet Res 29: 1983-89, 1968. 125

CARLSON J R, YOKOYAMA M T and DICKINSON E O: Induction of pulmonary edema and emphysema in cattle and goats with 3-methylindole. Science 176: 298-99, 1972. 126

EBERLY V E, TYLER W S and GILLESPIE J R: Cardiovascular parameters in emphysematous and control horses. J Appl Physiol 21: 883-89, 1966. 127

EHRLICH R and HENRY M C: Chronic toxicity of nirtogen dioxide. Arch Environ Health 17: 860-65, 1968. 128

FRASCA J M, AUERBACH O, PARKS V R and JAMIESON J D: Electron microscopic observations on pulmonary fibrosis and emphysema in smoking dogs. Exp Mol Pathol 15: 108-25, 1971. 129

FREEMAN G: The sub-acute NO_2 lesion of the rat lung. In: 9th American medical association air pollution medical research conference, 1968, pp 1-5. 130

FREEMAN G, CRANE S C, STEPHENS R J and FURIOSI N J: Pathogenesis of the nitrogen dioxid-induced lesion in the rat lung: A review and presentation of new observations. Am Rev Resp Dis 98: 429-43, 1968a 131

FREEMAN G, CRANE S C, STEPHENS R J and FURIOSI N J: Environmental factors in emphysema and a model system with NO_2. Yale J Biol Med 40: 566-75, 1968B. 132

FREEMAN G, CRANE S C, STEPHENS R J and FURIOSI N J: The subacute nitrogen dioxide-induced lesion of the rat lung. Arch Environ Health 18: 609-12, 1969. 133

FREEMAN G and HAYDON G B: Emphysema after low-level exposure to NO_2. Arch Environ Health 8: 125-28, 1964. 134

FREEMAN G, STEPHENS R J, CRANE S C and FURIOSI N J: Lesion of the lung in rats continuously exposed to two parts per million of nitrogen dioxide. Arch Environ Health 17: 181-92, 1968c 135

GILLISPIE J R and TYLER W S: Capillary and cellular changes in alveolar walls of emphysematous horse lungs. Am Rev Resp Dis 95: 484-90, 1967. 136

GILLISPIE J R, TYLER W S and EBERLY V E: Blood pH, O_2, and CO_2 tensions in exercised control and emphysematous horses. Am J Physiol 207: 1067-72, 1964. 137

GILLISPIE J R, TYLER W S and EBERLEY V E: Pulmonary ventilation and resistance in emphysematous and control horses. J Appl Physiol 21: 416-22, 1966. 138

GLAUSER E M and GLAUSER S C: The role of acidosis in the etiology of pulmonary emphysema. Proc Soc Exp Biol Med 131: 1034-37, 1969. 139

GOLDRING I P, GREENBURG L and RATNER I M: On the production of emphysema in Syrian hansters by aerosol inhalation of Papain. Arch Environ Health 16: 59-60, 1968. 140

GRAY E L: Oxides of nitrogen: Their occurrence, toxicity hazard. Arch Ind Health 19: 479-86, 1959. 141

GROSS P and deTREVILLE T P: Emphysema and pneumoconiosis. Arch Environ Health 18: 340-49, 1969. 142

GROSS P, deTREVILLE T P, BABYAK M A, KASCHAK M and TOLKER E B: Experimental emphysema. Arch Environ Health 16: 51-58, 1968A. 143

GROSS P, deTREVILLE T P, BABYAK M A, KASCHAK M and TOLKER E B: Experimental emphysema: effect of chronic nitrogen dioxide exposure and of papain on normal and pneumoconiotic lungs. Pub Health Serv 1787: 357-78, 1968B. 144

HAAGEN-SMIT L J, BRUNELLE M F and HARA J: Nitrogen oxide content of smokes from different types of tobacco. Arch Ind Health 20: 399-400, 1959. 145

HAMMOND E C, AUERBACH O, KIRMAN D and GARFINKEL L: Effects of cigarette smoking on dogs. Arch Environ Health 21: 740-53, 1970. 146

HAYDON G B, DAVIDSON J T, LILLINGTON G A and WASSERMAN K: Nitrogen dioxide-induced emphysema in rabbits. Am Rev Resp Dis 95: 797-805, 1967. 147

HAYDON G B, FREEMAN G and FURIOSI N J: Covert pathogenesis of NO_2 induced emphysema in the rat. Arch Environ Health 11: 776-83, 1965. 148

HENRY M C, EHRLICH R and BLAIR W H: Effect of nitrogen dioxide on resistance of squirrel monkeys to klebsiella pneumoniae infection. Arch Environ Health 18: 580-87, 1969. 149

HENRY M C, FINDLAY J, SPANGLER J and EHRLICH R: Chronic toxicity of NO_2 in squirrel monkeys. Arch Environ Health 20: 566-70, 1970. 150

HERNANDEZ J A, ANDERSON A E Jr, HOLMES W L and FORAKER A G: Pulmonary parenchymal defects in dogs following prolonged cigarette smoke exposure. Am Rev Resp Dis 93: 78-83, 1966. 151

INOH T and AVIADO D M: Cardiopulmonary effects of progestational agents in emphysematous rats. Chest 59: 659-66, 1971. 152

ITO H and AVIADO D M: Pulmonary emphysema and cigarette smoke. Arch Environ Health 16: 865-70, 1968. 153

ITO H and AVIADO D M: Prevention of pulmonary emphysema in rats by progesterone. J Pharmacol Exp Ther 161: 197-204, 1968. 154

Bibliography II-D

	Reprint
LOWRY T and SCHUMAN L M: "Silo-filler's disease" -- a syndrome caused by nitrogen dioxide. J Am Med Ass 162: 153-60, 1956.	155
MARCO V, MASS B, MERANZE D R, WEINBAUM G and KIMBEL P: Induction of experimental emphysema in dogs using leukocyte homogenates. Am Rev Resp Dis 104: 595-98, 1971.	156
MASS B, IKEDA T, MERANZE D R, WEINBAUM G and KEMBEL P: Induction of experimental emphysema. Cellular and species specificity. Am Rev Resp Dis 106: 384-91, 1972.	157
McLAUGHLIN R F, TYLER W S, EDWARDS D W, CRENSHAW G L, CANADA R O, FOWLER M A, PARKER E A and REIFENSTEIN G H: Chlorpromazine-induced emphysema. Am Rev Resp Dis 92: 597-608, 1965.	158
MITTMAN C (editor): Pulmonary emphysema and Proteolysis. Academic Press, New York, 1972, pp 1-562.	159
NANDI M, HERSHEL J, SLONE D, SHAPIRO S and LEWIS G P: Cadmium content of cigarettes. Lancet 2: 1329-30, 1969.	160
PALECEK F, PALECEKOVA M and AVIADO D M: Emphysema in immature rats. Arch Environ Health 15: 332-42, 1967.	161
REIF J S, RHODES W H and COHEN D: Canine pulmonary disease and the urban environment. Arch Environ Health 20: 676-83, 1970.	162
ROCKEY E E and SPEER F D: The ill effects of cigarette smoking on dogs. Int Surg 46: 520-30, 1966.	163
SHORE S R, and AVIADO D M: Hormones and pulmonary effects of tobacco. Arch Environ Health 19: 59-69, 1969.	164
SMITH J P, SMITH J C and McCALL A J: Chronic poisoning from cadmium fume. J Pathol 80: 287-96, 1960.	165
STEPHENS R J, FREEMAN G and EVANS M J: Ultrastructural changes in connective tissue in lungs of rats exposed to NO_2. Arch Intern Med 127: 873-83, 1971.	166
STRAWBRIDGE H T G: Chronic pulmonary emphysema (an experimental study). I Historical review. Am J Pathiol 37: 161-74, 1960A.	167
STRAWBRIDGE H T G: Chronic pulmonary emphysema (an experimental study). II. Spontaneous pulmonary emphysema in rabbits. Am J Pathiol 37: 309-31, 1960B.	168
STRAWBRIDGE H T G: Chronic pulmonary emphysema (an experimental study) III Experimental pulmonary emphysema. Am J Pathiol 37: 391-411, 1960C.	169
SYZGANOV A N, GOLOVIN Y A and TROITSKAYA E G: On the influence of tobacco smoke on the organs of respiration. Eksperimentalnay Khirurgiya 16: 23-26, 1971.	170
THURLBECK W M: Pulmonary emphysema. Am J Med Sci 246: 332-53, 1963.	171

Bibliography II-D

Reprint

VON OETTINGEN W F: The toxicity and potential dangers of nitrous fumes. Pub Health Bull 272: 1-34, 1941.

172

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING INHALATION OF POLLUTANTS AND INFECTION

Chronic bronchitis is a clinical disorder characterized by excessive mucus secretion. It may appear concurrently with pulmonary emphysema, so that the major problem in the diagnosis is to establish that bronchitis is the predominant disease.

As in pulmonary emphysema, cigarette smoking is one of the risk factors in the pathogenesis of chronic bronchitis. Two other risk factors, air pollution and infections, are discussed in this section. At the present time, it is not possible to rank these risk factors in the order of their importance.

The primary concern of this section is chronic bronchitis. The literature on postmortem, clinical and animal investigations relating to chronic bronchitis is reviewed here. Three bibliographic lists are appended:

No. 6. Chronic bronchitis: general aspects.

No. 7. Bronchial carcinoma.

No. 8. Air pollutants and lung disease.

The early cellular changes in the bronchial mucosa and secretion in chronic bronchitis have been confused with metaplasia, so that it is important to exclude consideration of neoplastic disease from the following paragraphs.

III-A. POSTMORTEM EXAMINATION

The basic histopathologic change of chronic bronchitis is generalized hypertrophy and hyperplasia of the mucus-secreting bronchial glands throughout the treachea and bronchi. There are also diffuse inflammatory changes consisting principally of increased number of mononuclear cells in the thickened trancheobronchial submucosa and metaplastic epithelial changes with loss of cilia (Reid 1954, 1960; [illegible], [illegible]; Marcatili et al., 1967; Thurlbeck and Angus 1967).

There are only two reports of postmortem examination and known smoking habits of patients with chronic bronchitis. Mitchell et al (1966) reported 64 autopsies, all but one subject having been smokers and 91% for more than 20 pack-years (no of pack daily x years). Niewoehner et al. (1972) reported 4 fatal cases of regional chronic bronchitis, all of the patients having been chronic smokers.

All the other postmortem observations compare the histological features of the bronchi of smokers and nonsmokers, most of them healthy, Chang (1956, 1957, 1958) in 105 random autopsies noted distended goblet cells in 25 out of 71 smokers (35%) but only in 6 out of 34 nonsmokers (17.6%). The average length of cilia was shorter than in nonsmokers and the smokers' epithelium was thicker than that of nonsmokers. The hypertrophy of the bronchial mucus glands, characteristic of chronic bronchitis, has been reported to be more frequent among smokers. The gland/wall ratio was significantly raised

in 35 heavy smokers, but there was no difference between 23 nonsmokers and 15 moderate (13ss than 20 cigarettes/day) smokers (Thurlbeck et al., 1963). A similar conclusion was arrived at in a larger group of cases, also in Canada like the previous group consisting of 40 nonsmokers and 111 smokers, including 58 heavy smokers (Thurlbeck and Angus, 1964). In another group, reported from England, the mean percentage volume of bronchial mucus glands was significantly greater in 106 smokers than in 73 nonsmokers (Dunnill and Ryder 1971; Ryder et al., 1971). In a smaller group, from Ohio, there was no difference in percentages of such glands between 11 smokers and 13 nonsmokers (Sobonya and Kleinerman, 1972). Ido et al. (1959) reported that percentages of goblet cells increased in light smokers but decreased in heavy smokers.

Squamous metaplasia of bronchial epithelium is commonly seen in various pathologic processes as a result of atypical epithelial regeneration. In 128 unselected autopsies, the general incidence of metaplasia was 32%; the highest incidence was 71% in patients with primary lung carcinoma and the next highest was 41% in patients with chronic inflammatory disease of the lung. In the same group, 39% of nonsmokers had metaplasia and 45% of smokers had a similar epithelial change (Weller, 1955). The subsequent reports show the incidence of metaplasia to be as follows:

Sanderad, 1958	8% of 58 smokers	54% of 39 nonsmokers
Cross et al., 1961	16% of 197 smokers	8% of 33 nonsmokers
Spain, 1969, 1970	65% of 52 smokers	50% of 36 nonsmokers

Auerbach et al. (1961; 1962a, b; 1968) have reported their results in terms of nature of the nucleus relevant to neoplastic changes. Their observations did not include those relating to bronchitis.

The incidence of goblet cell metaplasia is about equal in smokers and nonsmokers (Karpick et al., 1970). The proliferation of epithelial cells has been reported in the palate (Chapman and Redish, 1960) and larynx (Ryan et al., 1955) of smokers.

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING INHALATION OF POLLUTANTS AND INFECTION

A. POSTMORTEM EXAMINATION

Reprint

AUERBACH O, STOUT A P, HAMMOND E C and GARFINKEL L: Changes in bronchial epithelium in relation to cigarette smoking and in relation to lung cancer. N Engl J Med 265: 253-67, 1961. 173

AUERBACH O, STOUT A P, HAMMOND E C and GARFINKEL L: Changes in bronchial epithelium in relation to sex, age, residence, smoking and pneumonia. N Engl J Med 267: 111-19, 1962A. 174

AUERBACH O, STOUT A P, HAMMOND E C and GARFINKEL L: Bronchial epithelium in former smokers. N Engl J Med 267: 119-25, 1962B. 175

AUERBACH O, STOUT A P, HAMMOND E C and GARFINKEL L: Interrelationships among various histologic changes in bronchial tubes and in lung parenchyma. Am Rev Resp Dis 90: 867-876, 1968. 176

CHANG S C: Studies of bronchial epithelium from smokers and nonsmokers. Proc Am Ass Cancer Res 2: 99-100, 1956. 177

CHANG S C: Microscopic properties of whole mounts and sections of human bronchial epithelium of smokers and nonsmokers. Cancer 10: 1246-62, 1957. 178

CHANG S C: Studies of suberepithelial tissue of bronchi from smokers and non-smokers. Proc Am Ass Cancer Res 2: 286-87, 1958. 179

CHAPMAN I and REDISH C H: Tobacco-induced epithelial proliferation in human subject. Arch Path 70: 133-40, 1960. 180

CROSS K R, WALZ D V, PALMER G K and WARNER E D: A study of the tracheobronchial epithelium and changes related to smoking. J Iowa Med Soc 51: 137-40, 1961. 181

DUNNILL S and RUDEN R: A Quantative study of the relationship between chronic bronchitis emphysema and smoking. Chest 59 (5 Suppl): 355-65, 1971. 182

IDE G, SUNTZEEF V and COWDRY E V: A comparison of the histopathology of tracheal and bronchial epithelium of smokers and nonsmokers. Cancer 12: 473-84, 1959. 183

KARPICK R J, PRATT P C, ASMUNDSSON T and KILBURN K H: Pathological findings in respiratory failure. Goblet cell metaplasia, alveolar damage, and myocardial infarction. Ann Intern Med 72: 189-97, 1970. 184

MARCATILI S, BONO M D and ZUCCHETTO C: Comportamento dell'epitelio bronchiale in alcune bronco-pneumopatie chroniche. Riv Anat Patol Oncol 31: 308-30, 1967. 185

MITCHELL R S, RYAN S F, PETTY T L and FILLEY G: The significance of morphologic chronic hyperplastic bronchitis. Am Rev Resp Dis 93: 720-29, 1966. 186

NIEWOEHNER D E, KLEINERMAN J and KNOKE J D: Regional chronic bronchitis. Am Rev Resp Dis 105: 586-93, 1972. 187

REID L M: Pathology of chronic bronchitis. Lancet 1: 275-78, 1954. 188

Bibliography III-A

Reprint

REID L: Measurement of the bronchial mucous gland layer: a diagnostic yardstick in chronic bronchitis. Thorax 15: 132-41, 1960. 189

RYAN R F, McDONALD J R and DEVINE K D: The pathologic effects of smoking on the larynx. Arch Path 60: 472-80, 1955. 190

RYDER R C, DUNNILL M S and ANDERSON J A: A quantitative study of bronchial mucous gland volume, emphysema and smoking in a necropsy population. J Pathol 104: 59-71, 1971. 191

SANDERUD K: Squamous metaplasia of the respiratory tract epithelium. An autopsy study of 214 cases. Acta Path Microbiol Scand 43: 47-61, 1958. 192

SOBONYA R E and KLEINERMAN J: Morphometric studies of bronchi in young smokers. Am Rev Resp Dis 105: 768-75, 1972. 193

SPAIN D M: The distribution of tracheobronchial metaplasia (regenerative hyperplasia) (age, sex, cigarette smoking and relations to reid index) preliminary report. Pub Health Serv Pub 1879: 183-86, 1969. 194

SPAIN D M, BRADESS V A, TARTER R and MATERO A: Metaplasia of bronchial epithelium. JAMA 211: 1331-34, 1970. 195

THURLBECK W M and ANGUS G E: A distribution curve for chronic bronchitis. Thorax 19: 436-42, 1964. 196

THURLBECK W M and ANGUS G E: The variation of reid index measurements within the major bronchial tree. Am Rev Resp Dis 95: 551-55, 1967. 197

THURLBECK W M, FRASER R G and BATES D V: The correlation between pulmonary structure and function in chronic bronchitis, emphysema and asthma. Med Thorac 22:295-303, 1965. 198

THURLBECK W M, ANGUS G E and PARE J A P: Mucous gland hypertrophy in chronic bronchitis, and its occurrence in smokers. Br J Dis Chest 57: 73-78, 1963. 199

WELLER R W: Metaplasia of bronchial epithelium. A postmortem study. 768-74, 1955. 200

III-B. ANTEMORTEM STUDIES

Chronic bronchitis diagnosed clinically by measurements of lung function is seen both in smokers and in nonsmokers. Simonson (1965) reported a series from Sweden consisting of the following: of 30 males, 2 were nonsmokers and of 35 females 5 were nonsmokers. Half of the patients reported some allergy connection and one-third were exposed to dusts in their occupations.

A coordinated study in four Canadian cities included 216 patients with chronic bronchitis, 2 of whom were nonsmokers. In the follow-up data of the Toronto group, although the patients as a whole showed a decrease in ventilatory function and in diffusing capacity, 10 of the 44 patients had stopped smoking and a further 6 had reduced their cigarette consumption (Bates et al., 1966). No detectable improvement occurred following the reduction of smoking.

Of 260 patients with chronic bronchitis reported in Germany there was a higher proportion of nonsmokers than in other countries. Wendel (1968) counted 66 of these patients who were nonsmokers. In England, Simpson (1965) reported that 18 out of 157 patients were nonsmokers, and Caird et al. (1972) stated that out of 47 patients 18 were nonsmokers. In Egypt, Megaked (1966) reported that 8 out 65 bronchitic patients were non-smokers. In the United States, Massaro and Bottoms (1967) noted that 27 out of 327 patients were nonsmokers. The overall incidence of nonsmokers in all these reports is 13% of bronchitic patients.

Reports from Japan (Shiota et al., 1966), the United States (Burrows and Earle, 1969; Brinkmann and Block 1968, 1972) and England (Jones et al., 1967; Fletcher, 1968) indicated a high incidence of smokers among patients with chronic bronchitis but the exact figures were not given.

Bronchial biopsy has been performed in patients with chronic bronchitis. There was a higher incidence of mucus gland hypertrophy in smokers than in nonsmokers (Megahed et al., 1967). A few patients with regional bronchitis have been described but the number is too small to allow evaluation of significance of smoking (Anthonisen et al., 1968; Niewoehner et al., 1972).

BIBLIOGRAPHY

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING, INHALATION OF POLLUTANTS AND INFECTION

B. ANTEMORTEM STUDIES

Reprint

ANTHONISEN N R, BASS H, ORIOL A, PLACE R E G, and BATES D V: Regional lung function in patients with chronic bronchitis. Clin Sci 35: 495-511, 1968. 201

BATES D V, GORDON C A, PAUL G I, PLACE R E G, SNIDAL D P and WOOLF C R: Chronic bronchitis. Report of the third and fourth stages of the co-ordinated study of chronic bronchitis in the department of verterns affairs, Canada. Med Serv J Can :1-59, 1966. 202

BRINKMAN G L, BLOCK D L: The prognosis in chronic bronchitis. Pub Health Serv 1717: 317-26, 1968. 203

BRINKMANN G L, BLOCK D L: Chronic bronchitis in a working population. J Occup Med 14: 825-27, 1972. 204

BURROWS B and EARLE R H: Prediction of survival in patients with chronic airway obstruction. Am Rev Resp Dis 99: 865-871, 1969. 205

CAIRD F I and AKHTAR A J: Chronic respiratory disease in the elderly. A population study. Thorax 27: 764-68, 1972. 206

FLETCHER C M: Prognosis in chronic bronchitis. Pub Health Service 1717: 309-15, 1968. 207

JONES N L, BURROWS B and FLETCHER C M: Serial studies of 100 patients with chronic airway obstruction in London and Chicago. Thorax 22: 327-35, 1967. 208

MASSARO D and BOTTOMS L: Epidemiology of chronic bronchitis. Med Times 95: 121-28, 1967. 209

MEGAHED G E: The role of smoking in chronic bronchitis in Egyptians. J Egypt Med Ass 49: 313-28, 1966. 210

MEGAHED G E, SENNA G A, EISSA M H, SALEH S Z and EISSA H A: Smoking versus infection as the aetiology of bronchial mucous gland hypertrophy in chronic bronchitis. Thorax 22: 271-78, 1967. 211

NIEWOEHNER D E, KLEINERMAN J and KNOKE J D: Regional chronic bronchitis. Am Rev Resp Dis 105: 586-93, 1972. 212

SHITO K, HAMADA A, YASUTARO Y M, EMURA M, MITANI K, MATSUDA M, INOUE T, SAWAL M, KAWAMURA S and OKUBO M: Studies on chronic bronchitis in Osaka. Jap J Med 6: 105-6, 1967. 213

SIMONSSON B G: Clinical and physiological studies on chronic bronchitis. Acta Allergologica 20: 257-300, 1965. 214

SIMPSON T: Chronic bronchitis and emphysema with special reference to prognosis. Br J Dis Chest 62: 57-79, 1968. 215

WENDEL V H: Zur bedeutung des rauchens fur die chronische bronchitis. Zeit Ges Ann Med 23: 147-51, 1968. 216

III-C. EXAMINATION OF SPUTUM

There is an increase in the amount of expectoration in patients with chronic bronchitis. The observations relating to cigarette smoking consist of the cellular components of the sputum. Vassar et al. (1960) reported an increase in fluorescent histiocytes in the sputum of cigarette smokers which were absent in that of nonsmokers. They suggested that the fluorescence might be due to the presence of polycyclic hydrocarbons bound to the lipid in the cytoplasm of the histiocyte. Roque and Pickren (1968) performed a histochemical study of lung biopsies. In the histiocytes (also known as alveolar macrophages) of smokers there was a loss of oxidoreductases and hydrolases that was directly proportional to the amount of fluorescent material stored in the cells.

Masin and Masin (1966) examined sputum specimens and observed an increase in the proportion of lipophages in the smokers as compared with the nonsmokers. They explained the difference as due to a combined effect of irritation of the alveolar lining, increased turnover of alveolar cells with increased injury to macrophages and shift in the relative proportion of lipophages. Alveolar macrophages obtained by endobronchial lavage of cigarette smokers and nonsmokers were examined with the electron microscope (Pratt et al., 1971). In smokers the inclusions are heterogeneous and measure from 0.1 to 20 μ in diameter; the inclusions in nonsmokers are mostly round or oval and measure from 0.1 to 2.0 μ.

There is an increase in incidence of metaplasia of bronchial epithelial cells in the sputum of smokers (Robbins, 1966; Fullmer, 1968; Nasiell, 1968; Rimingen, 1968). Since metaplasia also occurs in nonsmokers, it is

not possible to attribute to smoking the presence of cells thus affected. Fullmer et al., (1969) observed an increase in incidence of bronchial and bronchiolar spirals, fibrils and casts in smokers who were suffering from chronic bronchitis as compared with nonsmokers.

The other techniques for the examination of sputum concern sputum purulence (Miller, 1963), protein turnover (Bonomo and D'Addabbo, 1964), electrolyte content (Nicolas, 1964) and concentration of neuraminic acid (Reid, 1967). The influence of smoking on these parameters has not been investigated.

BIBLIOGRAPHY

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING, INHALATION OF POLLUTANTS AND INFECTION

C. EXAMINATION OF SPUTUM

Reprint:

BONOMO L and D'ADDABBO A: Albumin turnover and loss of protein into the sputum in chronic bronchitis. Clinica Chemica Acta 10: 214-22, 1964. 217

FULLMER C D: Microscopic observations of sputum of chronic cigarette smokers. Rocky Mt Med J 65: 13, 1968. 218

FULLMER C D, SHORT J G, ALLEN A and WALKER K: Sputum of chronic cigarette smokers. Rocky Mt Med J 66: 42-46, 1969. 219

MASIN F and MASIN M: Frequencies of alveolar cells in concentrated sputum specimens related to cytologic classes. Acta Cytologica 10: 362-67, 1966. 220

MILLER D L: Study of techniques for the examination of sputum in a field survey of chronic bronchitis. Am Rev Resp Dis 88: 473-83, 1963. 221

NASIELL M: Sputum-cytologic changes in smokers and non-smokers in relation to chronic inflammatory lung diseases. Acta Pathol Microbiol Scand 74: 205-13, 1968. 222

NICOLAS R: Klinisch-experimentelle sputumuntersuchungen bei chronischer bronchitis. Medicina Thoracalis 21: 223-55, 1964. 223

PRATT S A, SMITH M H, LADMAN A J and FINLEY T N: The ultrastructure of alveolar macrophages from human cigarette smokers and nonsmokers. Scand J Clin Lab Invest 24: 331-38, 1971. 224

REID L: Mucus secretion and chronic bronchitis. Medicina Thoracalis 24: 40-43, 1967. 225

RIMINGTON J: Smoking, sputum, and lung cancer. Br Med J 1: 732-34, 1968. 226

ROBBINS W T: Bronchial epithelium in smoking and non-smoking college students. J Am Coll Health Assoc 14: 265-66, 1966. 227

ROQUE A L and PICKREN J W: Enzymatic changes in fluorescent alveolar macrophages of the lungs of cigarette smokers. Acta cytologica 420-29, 1968. 228

VASSAR P S, CULLING C and SAUNDERS A M: Fluorescent histiocytes in sputum related to smoking. Arch Pathol 70: 649-52, 1960. 229

III-D. AIR POLLUTANTS AS A RISK FACTOR

The role of air pollutants in the pathogenesis of chronic bronchitis is discussed in the articles listed in bibliographic list no. 8. Briefly, the association of this condition with air pollutants is similar to that with cigarette smoking. There is a parallel relationship between the incidence of chronic bronchitis and either the degree of pollution in the air or the amount of cigarette smoking (Anderson 1962).

The incidence of chronic bronchitis in the general population has been correlated with the following indices of air pollution. Fairbairn and Reid (1958) reported that among London postmen disablement and death were related to the frequency of fog and presumably the level of air pollution. Schoettlin (1962) observed that the prevalence of chronic bronchitis among elderly males was higher among those exposed to five occupational factors: cooking fats, gasoline and oils, coal dust and welding fumes. Among American male college students the incidence of chronic bronchitis detected by evaluation of respiratory function was correlated significantly with ambient temperature (Spodnik et al., 1966). Levels of sulfur dioxide in the air showed a positive correlation with incidence of respiratory illness in the United States (McCarroll et al., 1967; Heimbach, 1971).

The importance of air pollution and cigarette smoking has been assessed by some investigators. Winkelstein (1969), Motley (1971),

Motley and Yanda (1966) and Cohen et al. (1972) have the opinion that cigarette smoking is more significant than air pollution in causing chronic bronchitis. Their evidence is not based on a comparison with subjects free from exposure to pollutants. The experience of Phelps and Koike (1962) in the Tokyo-Yokohama episode of asthmatic bronchitis is unique in that American soldiers who were heavy smokers were exposed to air pollutants. After they were transferred to the United States, although they continued smoking, their bronchitis was relieved. In this episode, air pollution is more important than cigarette smoking in causing bronchitis.

BIBLIOGRAPHY

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING, INHALATION OF POLLUTANTS AND INFECTION

D. AIR POLLUTANTS AS A RISK FACTOR

Reprint

ANDERSON R J: Epidemiologic studies of air pollution. Dis Chest 42: 474-81, 1962. 230

COHEN C A, HUDSON A R, CLAUSEN J L and KNELSON J H: Respiratory symptoms, spirometry, and oxident air pollution in nonsmoking adults. Am Rev Resp Dis 105: 251-61, 1972. 231

FAIRBAIRN A S and REID D D: Air pollution and other local factors in respiratory disease. Br J Prev Soc Med 12: 94-103, 1958. 232

HEIMBACH J A Jr: The correlation of polluted air with tree growth and lung disease in humans. Compr Biol Med 1: 243-53, 1971. 233

McCARROLL J, CASSELL E J, WOLTER D W, MOUNTAIN J D, DIAMOND J R and MOUNTAIN I M: Health and the urban environment. V. Air pollution and illness in a normal urban population. Arch Environ Health 14: 178-83, 1967. 234

MOTLEY H L: Clinical aviation and aerospace medicine. Environmental air pollution effect on pulmonary function. Aerosp Med 42: 1108-10, 1971. 235

MOTLEY H L and YANDA R: Environmental air pollution, emphysema and ionized air. Dis Chest 50: 343-52, 1966. 236

PHELPS H W and KOIKE S: Tokyo-Yokohama Asthma. The rapid development of respiratory distress presumable due to air pollution. Am Rev Resp Dis 86: 55-63, 1962. 237

SCHOETTLIN C E: The health effect of air pollution on elderly males. Am Rev Resp Dis 86: 878-97, 1962. 238

SPODINK M J Jr, CUSHMAN G D, KERR D H, BLIDE R W and SPICER W S: Effects of environment on respiratory function. Arch Environ Health 13: 243-54, 1966. 239

WINKELSTEIN W Jr, and KANTOR S: Respiratory symptoms and air pollution in an urban population of northeastern United States. Arch Environ Health 18: 760-67, 1969. 240

III-E. INFECTION AS A RISK FACTOR

The basic lesion in chronic bronchitis is inflammation, which is largely due to pathogens. The infectious process may either be the primary cause of the inflammation or may supercede the initial irritation of the bronchial mucosa by chemical substances. There are defence mechanisms which protect the bronchial passages from bacterial or viral infections (see reviews by Green, 1968 a, b, and Rylander, 1969). The process of clearance of bronchial passages is accomplished by the ciliated epithelium and the mucus-secreting goblet cells. The effect of cigarette smoking on mucociliary clearance is discussed in Section VI. The next paragraphs discuss the influence of cigarette smoking on the bronchial infections, which in turn would lead to chronic bronchitis.

The incidence of the common cold is not higher in smokers than in nonsmokers (Kler, 1945). Amon 143 allergic subjects between 18 and 35 years of age, who were challenged with infectious secretions taken from patients with a common cold, 45% developed colds as compared with 31% among 693 nonallergic individuals, who were inoculated in the same way. Amon both groups of subjects, 35% of smokers and 34% of nonsmokers developed colds, indicating that smoking did not influence the susceptibility to the common cold (Dowling et al., 1957). This is the most important evidence that smoking does not increase the susceptibility to the common cold.

Prevalence studies have produced the opposite conclusion. On the basis of symptoms of acute repiratory infections, the following groups show

a higher incidence among smokers than nonsmokers: 118 adults residing in Cleveland (Boake, 1958); 175 student nurses in Canada (Parnell et al., 1966); 191 high school students in New Jersey (Haynes et al., 1966); 1,811 male college students in South Carolina (Finklea et al., 1969).

There are other observations relating to the influence of smoking on the incidence of bronchial infections. Air pollution has been shown by Douglas and Waller (1966) to relate to frequency of respiratory infection in children residing in London. The antibacterial activity of the saliva is enhanced by thiocyanate ion which may be absorbed from cigarette smoke (Courant, 1967). Patients with pulmonary emphysema show an elevation of immunoglobulin A(Ig A) in the blood, which has been interpreted as a sign of the presence of bronchopulmonary infection (Biegel and Krumholz, 1968). The concentration of immunoglobulin A in the saliva is also elevated in patients with chronic pulmonary disease, but this was not influenced by cigarette smoking (Lewis et al., 1970). In the same study cigarette smoking suppressed production of immunoglobulin A in the saliva of normal subjects. These observations on immunoglobulin do not explain the association between cigarette smoking and respiratory infections.

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING INHALATION OF POLLUTANTS AND INFECTION

E. INFECTION AS A RISK FACTOR

Reprint

BIEGEL A A and KRUMHOLZ R A: An immunoglobulin abnormality in pulmonary emphysema. Am Rev Resp Dis 97: 217-22, 1968. 241

BOAKE W C: A study of ilness in a group of Cleveland families. XVIII. Tobacco smoking and respiratory infections. N Engs J Med 259: 1245-49, 1958. 242

COURANT P: The effect of smoking on the antilactobacillus system in saliva. Odontol Revy 18: 251-61, 1967. 243

DOUGLAS J W B and WALLER R E: Air pollution and respiratory infection in children. Br J Prev Soc Med 20: 1-8, 1966. 244

DOWLING H F, JACKSON G G and INOUYE T: Transmission of the experimental common cold in volunteers. II. The effect of certain host factory upon susceptibility. J Lab Clin Med 50: 516- 25, 1957. 245

FINKLEA J F, SANDIFER S H and SMITH D D: Cigarette smoking and epidemic influenza. Am J Epidemiol 90: 290-99, 1969. 246

GREEN G M: Pulmonary antibacterial mechanisms and the pathogenesis of pulmonary disease. Yale J Biol Med 40: 414-29, 1968A. 247

GREEN G M: Pulmonary clearance of infectious agents. Ann Rev Med 19: 315-36, 1968B. 248

HAYNES W F Jr, KRSTULOVIC V J and BELL A L L: Smoking habit and incidence of respiratory tract infections in a group of adolescent males. Am Rev Resp Dis 93: 730-35, 1966. 249

KLER J H: An analysis of colds in industry. Trans Am Acad Ophthalmol Otolaryngol 201-7, 1945. 250

LEWIS D M, LAPP N L and BURRELL R: Quantitation of secretory immunoglobulin A in chronic pulmonary disease. Am Rev Resp Dis 101: 55-61, 1970. 251

PARNELL J L, ANDERSON D O and KINNIS C: Cigarette smoking and respiratory infections in a class of student nurses. New Engl J Med 274: 979-84, 1966. 252

RYLANDER R: Environmental air pollutants and lung defense to airborne bacteria. Pub Health Serv Pub 1879: 297-304, 1969. 253

III-F. ANIMAL EXPERIMENTS RELATING TO CHRONIC BRONCHITIS

There is no available model in the laboratory which mimics the pathological and functional features of the human form of chronic bronchitis. The reported experiments pertain to one of several underlying processes in chronic bronchitis, such as mucus secretion, bronchial epithelial changes, nature of the alveolar lining and the influence of infection (see reviews by Pattle, 1958, 1965 and Green, 1968 and 1969). There are no reported measurements of pulmonary function in these animals to validate the claim that the experiments can be applied to elucidate the effects of cigarette smoking in man.

1. Rabbit. Proetz (1939) reported the first observations on the effect of cigarette smoke on the airways of the rabbit. By visual examination he noted the accumulation of tar, chiefly in the nasal cavity. Holland et al. (1958, 1963) impregnated cigarettes with radioactive arsenic to trace absorption of smoke in the rabbit. Exposure for one to two years caused pathological changes in the respiratory epithelium of the nose and tracheobronchial mucosa, but no measurements were made prior to sacrificing the animals. The remaining observations in the rabbit relate to the alveolar macrophages investigated in vitro (Heese and Myrvik, 1967; Myrvik and Evans, 1967; Weissbecker et al., 1969). The water-soluble constituents of cigarette smoke depress protein synthesis in rabbit alveolar cells (Yeager, 1969). The depressant action of cigarette smoke on phagocytic activity of alveolar macrophages may be prevented by gluthathione and cysteine (Green and Carolyn, 1967; Green, 1968 a, b).

2. Guinea pig. Rylander (1968, 1969) used the guinea pig to investigate the pulmonary defence mechanism against airborne bacteria. Animals exposed to cigarette smoke showed a reduction in the number of radioactive bacteria killed, as compared with the controls. This was interpreted as an effect of smoke on the mucus flow which clears the lung. There was no difference in the reduction of viable bacteria, indicating that the efficiency of the bactericidal mechanisms had not been impaired. In a subsequent report, Rylander (1971) described a reduction in the number of free lung cells in the fluid used for lavaging the airways. However, after two to four weeks of exposure there was an increase in the number of macrophages. This biphasic response indicates a tolerance to the reduction of cells in response to cigarette smoke. An increase in the number of pulmonary cells from chronic exposure has been reported by Flint et al. (1971). The depression of oxidative phosphorylation of pulmonary cells noted by Kyle and Riesen (1970) after 2 1/2 days' exposure needs to be examined in animals exposed for several weeks.

3. Rat. Exposure of the rat to cigarette smoke for six weeks produced an increase in the number of goblet cells in the trachea and intrapulmonary airways (Lamb and Reid, 1969). The effect cannot be induced by inhalation of extremes of temperature, indicating that this is not the important factor in smoke which increases the number of goblet cells (Jones et al., 1971). The addition of phenylmethyloxadiazole to the tobacco protected the rat from the increase in goblet cell count. This was the first effective means of protection found against changes produced in bronchial epithelium by tobacco smoke (Jones et al., 1972). The condition of pulmonary

macrophages in response to air pollutants other than cigarette smoke has been studied by Gross et al. (1969).

4. Mouse. Leuchtenberger et al. (1958, 1960) and Leuchtenberger and Leuchtenberger (1965) reported the cytochemical and cytological alteration in the bronchi of mice exposed to cigarette smoke. The presence of bronchitis was diagnosed by appearance of proliferative epithelial changes and metaplasia. These changes relate to carcinogenesis rather than to bronchitis. There is a decrease in bacterial clearance following an acute exposure to cigarette smoke (Laurenzi et al., 1963). There is an increase in susceptibility to naturally acquired infection of the respiratory tract in mice exposed to cigarette smoke (Wynder et al., 1968). In experiments on mice challenged with Klebsiella pneumoniae or Diplococcus pneumoniae, the decrease in resistance was shown to be transitory. When the time interval between smoke exposure and infectious challenge was lengthened from 1 to 48 hours, there was no demonstrable decrease in resistance to respiratory infection (Spurgash et al., 1968).

5. Dog. Auerbach et al. (1967) and Frasca et al. (1968 a, b) reported the histological and ultrastructural changes in the bronchial epithelium of dogs exposed to cigarette smoke for 24 to 421 days. The atypical nuclei noted in the epithelium do not relate to chronic bronchitis and are beyond the scope of this review.

BIBLIOGRAPHY

III. CHRONIC BRONCHITIS: CONCURRENCE OF CIGARETTE SMOKING, INHALATION OF POLLUTANTS AND INFECTION

F. ANIMAL EXPERIMENTS RELATING TO CHRONIC BRONCHITIS

Reprint

AUERBACH O, HAMMOND E C, KIRMAN D, GARFINKEL L and STOUT A P: Histologic changes in bronchial tubes of cigarette-smoking dogs. Cancer 20: 2055-66, 1967. 254

FLINT G L, MAXWELL K W and RENZETTI A D: Influence of cigarette smoke on guinea pigs. Effect on pulmonary cells and serum antitrypsin levels. Arch Environ Health 22: 366-69, 1971. 255

FRASCA J M, AUERBACH O, PARKS V R and JAMIESON J D: Electron microscopic observations of the bronchial epithelium of dogs. I. Control Dogs. Exp Mol Pathol 9: 363-79, 1968A. 256

FRASCA J M, AUERBACH O, PARKS V R and JAMIESON J D: Electron microscopic observations of the bronchial epithelium of dogs. II. Smoking dogs. Exp Mol Pathol 9: 380-99, 1968B. 257

GREEN G M: Protection of alveolar macrophages from the cytotoxic activity of cigarette smoke by glutathione and cysteine. J Clin Invest 47: 42a-43a, 1968A. 258

GREEN G M: Pathophysiology of the alveolar macrophage system. Public Health Serv 1786: 463-80, 1968B. 259

GREEN G M: Cigarette smoke: protection of alveolar macrophages by glutathione and cysteine. Science 162: 810-11, 1968C. 260

GREEN G M: The response of the alveolar macrophage system to host and environmental changes. Arch Environ Health 18: 548-50, 1969. 261

GREEN G M and CAROLIN D: The depressant effect of cigarette smoke on the in vitro antibacterial activity of alveolar macrophages. N Engl J Med 276: 421-27, 1967. 262

GROSS P, deTREVILLE T P, TOLKER E B, KASCHAK M and BABYAK M A: The pulmonary macrophage response to irritants. Arch Environ Health 18: 174-85, 1969. 263

HEISE E R and MYRVIK: Secretion of lysozyme by rabbit alveolar macrophages in vitro. J Reticuloendothel Soc 4: 510-23, 1967. 264

HOLLAND R H, KOZLOWSKI E J and BOOKER L: The effect of cigarette smoke on the respiratory system of the rabbit. Cancer 16: 612-15, 1963. 265

HOLLAND R H, WILSON R H, MORRIS D, McCALL M S and LANZ H: The effect of cigarette smoke on the respiratory system of the rabbit. Cancer 11: 709-12, 1958. 266

JONES R, BAETJER A M and REID L: Effect of extremes of temperature and humidity on the goblet cell count in the rat airway epithelium. Br J Ind Med 28: 369-73, 1971. 267

JONES R, BOLDUC P and REID L: Protection of rat bronchial epithelium against tobacco smoke. Br Med J 2: 142-44, 1972. 268

KYLE J L and RIESEN W H: Stress and cigarette smoke effects on lung mitochondrial phosphorylation. Arch Environ Health 21: 492-97, 1970. 269

LAMB D and REID L: Goblet cell increase in rat bronchial epithelium after exposure to cigarette and cigar tobacco smoke. Br Med J 1: 33-35, 1969. 270

LAURENZI G A, GUARNERI J L, ENDRIGA R B and CAREY J P: Clearance of bacteria by the lower respiratory tract. Science 142: 1572-73, 1963. 271

LEUCHTENBERGER V C and LEUCHTENBERGER R: Kumulative wirkung von zigaretenrauch-inhalation und influenza-virus-infektion bei der entstehung von atypischen proliferationen im bronchialepithel von mausen. Oncologia 19: 81-104, 1965. 272

LEUCHTENBERGER C, LEUCHTENBERGER R and DOOLIN P F: A correlated histological cytological and cytochemical study of the tracheobronchial tree and lungs of mice exposed to cigarette smoke. I. Bronchitis with atypical epithelial changes in mice exposed to cigarette smoke. Cancer 11: 490-526, 1958. 273

LEUCHTENBERGER C, LEUCHTENBERGER R, ZEBRUN W and SHAFFER P: A Correlated histological cytological and cytochemical study of the tracheobronchial tree and lungs of mice exposed to cigarette smoke. II. Varying responses of major bronchi to cigarette smoke, absence of bronchogenic carcinoma after prolonged exposure, and disappearance of bronchial lesions after cessation of exposure. Cancer: 13: 721-32, 1960. 274

MYRVIK Q N and EVANS D G: Metabolic and immunologic activities of alveolar macrophages. Arch Environ Health 14: 92-96, 1967. 275

PATTLE R E: Properties, function, and origin of the alveolar lining layer. Proc R Soc Biol 148: 217-40, 1958. 276

PATTLE R E: Surface lining of lung alveoli. Physiol Rev 45: 48-79, 1965. 277

PROETZ A: Some preliminary experiments in the study of cigarette smoke and its effects upon the respiratory tract. Ann Otol 48: 176-94, 1939. 278

RYLANDER R: Pulmonary defence mechanisms to airborne bacteria. Acta Physiol Scand Suppl 306: 1-89, 1968. 279

RYLANDER R: Alterations of lung defence mechanisms against airborne bacteria. Arch Environ Health 18: 551-55, 1969. 280

RYLANDER R: Free lung cell studies in cigarette smoke inhalation experiments. Scand J Resp Dis 52: 121-28, 1971. 281

SPURGASH A, EHRLICH R and PETZOLD R: Effect of cigarette smoke on resistance to respiratory infection. Arch Environ Health 16: 385-91, 1968. 282

WEISSBECKER L, CARPENTER R D, LUCHSINGER P C and OSDENE T S: In vitro alveolar macrophage viability. Effect of gases. Arch Environ Health 18: 756-59, 1969. 283

WYDNER E L, TAGUCHI K T, BADEN V and HOFFMANN D: Tobacco carcinogenesis. IX. The effect of cigarette smoke on respiratory tract of mice after passive inhalation. Cancer 21: 134-53, 1968. 284

Bibliography III-F

Reprint

YEAGER H Jr: Alveolar cells: depressant effect of cigarette smoke on protein synthesis. Proc Soc Exp Biol Med 131: 247-50, 1969. 285

IV. PULMONARY EMPHYSEMA-BRONCHITIS COMPLEX

Pulmonary emphysema-bronchitis complex, also known as chronic obstructive pulmonary disease, is discussed in this section separately from the sections dealing with its individual components (Sections II and III). It has been the practice of the United States Public Health Service to base their mortality statistics on a combination of pulmonary emphysema and chronic bronchitis even though separate death rates are available. It appears that combining the two entities under a single name has improved the results of statistical analysis in establishing the high incidence of deaths from pulmonary disease among smokers as compared with nonsmokers. The publications relating to the pulmonary emphysema-bronchitis complex are contained in additional bibliographic lists as follows:

No. 9. Pulmonary emphysema-bronchitis complex: etiology and pathology.

No. 10. Pulmonary emphysema-bronchitis complex: clinical studies.

Most of the publications in the above-mentioned lists emphasize the difference between the two entities, but the practice of combining both in mortality statistics has not been discontinued in the United States and has also been adopted in foreign countries.

IV-A. MORTALITY STATISTICS IN THE UNITED STATES

In 1958 Dorn reported the mortality experience of male policy holders of U. S. Government Life Insurance during the 2 1/2-year period 1954-1956. The death rate for persons who had smoked regularly was 36% greater than that for persons who had never smoked. Expressed in another way, with 1.00 as the death rate of nonsmokers, , that of smokers was 1.36. The mortality ratios for the diseases of the lung were as follows: cancer of the lung, 9.85, chronic obstructive pulmonary disease, 3.27. It was on this basis that the United States Public Health Service founded their conclusion that cigarette smoking causes cancer of the lung and chronic obstructive pulmonary disease. The mortality ratio of deaths from coronary heart disease was 1.63 and it is on this lower ratio that cigarette smoking was regarded as a risk factor. It will be noted that the mortality ratio of chronic lung disease is closer to that of heart disease than to that of lung carcinoma, so that it would have been more logical to draw a similar conclusion for chronic lung disease and heart disease. The subsequent publications of Dorn (1959, 1960, 1961), Kahn (1961) and Weir and Dunn (1970) recounted these mortality ratios and called attention to the declining death rate from disease of the respiratory system since 1900 (from 26% in 1900 to 8% in 1959). However, during the past decade the death rate increased significantly for a group of chronic respiratory diseases, including chronic bronchitis, emphysema, fibrosis and pneumonia.

The second mortality study, in which 1,078,894 persons were enrolled, was conducted by the American Cancer Society in 1959 and 1960. The mortality rate was higher for smokers than for nonsmokers. The mortality ratio for the pulmonary emphysema-bronchitis complex among smokers as compared with nonsmokers was 3.27 (Hammond and Horn, 1958; Hammond, 1959, 1964, 1966). The details of the statistical analysis of the mortality figures are contained in the publications relating to Smoking and Health. The regional analyses have been published separately for Georgia (Hammond and Letton, 1965), Illinois (Hammond and Street, 1964), Iowa (Hammond and Stocks, 1964), Kansas (Hammond et al., 1964), Minnesota (Hammond et al., 1965), Missouri (Hammond and Wilson, 1965), New York State (Hammond et al., 1965), and Ohio (Hammond and Gerber, 1965). The similarities in the mortality statistics of these areas have been emphasized but their dissimilarities have been ignored.

BIBLIOGRAPHY

IV. PULMONARY EMPHYSEMA-BRONCHITIS COMPLEX

A. MORTALITY STATISTICS IN THE UNITED STATES

	Reprint
DORN H F: The mortality of smokers and nonsmokers. Am Stat Ass Proc Soc Stat Sec 34-71, 1958.	286
DORN H F: Tobacco consumption and mortality from cancer and other diseases. Public Health Report 74: 581-73, 1959.	287
DORN H F: Tobacco consumption and mortality from cancer and other diseases. Acta Un Int Cancer 16: 1653-65, 1960.	288
DORN H F: The increasing mortality from chronic respiratory diseases. Am Stat Ass Proc Soc Stat Sec 148-52, 1961.	289
HAMMOND E C: Discussion. Am Stat Ass Proc Soc Stat Sec 60-64, 1959.	290
HAMMOND E C: Smoking in relation to mortality and morbidity. Findings in first thirty-four months of follow-up in a prospective study started in 1959. J Natl Cancer Inst 32: 1161-88, 1964.	291
HAMMOND E C: Smoking in relation to the death rates of one million men and women. Natl Cancer Inst Monogr 19: 127-204, 1966.	292
HAMMOND E C, BERGLUND L and KASLOW R: Smoking habits and disease in Minnesota. Minn Med 48: 44-49, 1965.	293
HAMMOND E C, FENT L S, REED D C and WILSON J L: Smoking habits and health in Kansas and other central states. J Kansas Med Soc 65: 586-90, 1964.	294
HAMMOND E C and GERBER L F: Smoking habits and disease in Ohio: Ohio State Med J 61: 134-37, 1965.	295
HAMMOND E C and HORN D: Smoking and death rates -- report on forty-four months of follow-up of 187,783 men. JAMA 166: 1298-1308, 1958.	296
HAMMOND E C and LETTON A H: Smoking habits and health in Georgia and other Southern states. J Med Assoc Ga 54: 278-81, 1965.	297
HAMMOND E C and STOCKS A: Smoking habits and health in Iowa and neighboring states. J Iowa Med Soc 54: 563-67, 1964.	298
HAMMOND E C and STREET E C: Smoking habits and disease in Illinois. Illinois Med J 126: 661-65, 1964.	299
HAMMOND E C, GRIETHUYSEN T H V, DIBELER J B, SNEDDON A M and HALLIGAN W: Smoking habits and disease in New York State. New York State J Med 65: 2557-61, 1965.	300
HAMMOND E C and WILSON O: Smoking habits and disease in Missouri. Missouri Med 62: 109-12, 122, 1965.	301

Bibliography IV-A

Reprint

JAMES G and ROSENTHAL T: Tobacco and health. Charles C Thomas, Springfield, 1961, pp172-90. 302

KAHN H A: The Dorn study of smoking and mortality among U.S. veterans: report on eight and one-half years of observations. Natl Cancer Inst Monogr 19: 1-125, 1966. 303

MILLS C A: Tobacco smoking: Some hints of its biologic hazards. Ohio State Med J 46: 1165-70, 1950. 304

WEIR J M and DUNN J E Jr: Smoking and mortality: a prospective study. Cancer 25: 105-12, 1970. 305

IV-B. MORTALITY STATISTICS IN FOREIGN COUNTRIES

The frequency of fatal chronic pulmonary disease varies in different countries (Reid and Fletcher, 1971). There is a wide range in the sex ratio of death in males and females, from 2.0 in Japan to 9.9 in Finland, with Canada, Great Britain and the United States between the extremes. These variations do not relate entirely to differences in cigarette consumption but indicate the association of other factors, some identified and others unidentified.

1. Canada. A questionnaire sent to 92,000 veterans from 1956 to 1962 revealed a higher death rate from pulmonary disease among both smokers and nonsmokers (Canadian Department of National Health and Welfare, 1966; Best et al.[a, b, c], 1967). The mortality ratio for all smokers as compared with nonsmokers was 1.33. The ratios for specific diseases were as follows: lung cancer, 14.91; bronchitis and emphysema, 8.71; and coronary heart disease, 1.60. The results of this survey were included in the report of the United States Public Health Service. As in the United States, an increasing number of deaths in Canada during the past decade have been due to chronic obstructive disease. The provincial statistics vary in the assignment of deaths due to pulmonary emphysema. Manitoba having the highest proportion of deaths caused by emphysema and Ontario the highest proportion of deaths due to chronic bronchitis. Cigarette consumption when expressed per person (15 years of age and over) does not correlate with the distribution of chronic pulmonary obstructive disease (Anderson, 1963, 1968).

2. Great Britain. The results of a questionnarie sent to 59,600 physicians indicate a relationship between cigarette smoking and mortality rates (Doll and Hill, 1964 a, b). A total number of 111 physicians died of chronic bronchitis. The standardized death rates per 1,000 were as follows: all men, 0.34; nonsmokers, 0.05; all smokers, 0.37; cigarette smokers, 0.51; mixed smokers, 0.33; and pipe or cigar smokers, 0.15. The death rate of smokers is higher than that of nonsmokers. It was recognized by the authors in an earlier report (1956) that some of the excess mortality among cigarette smokers might be due to a tendency to diagnose chronic bronchitis rather than some other respiratory disease in patients with a chronic cough.

3. Israel. The mortality statistics attributed to chronic bronchitis or to emphysema from 1960 to 1964 have been reviewed by Cohen (1967). There has been a rise in such deaths, which are more frequent among immigrants from Africa and Asia than among those from Europe. The author attempted to relate the differences among immigrants to smoking habits surveyed in 1958. The heavy smokers, those using more than 20 cigarettes daily, constituted 27% of all smokers emigrating from Asia and Africa, and 17% of those from Europe. The interpolation of results from another decade has been questioned. Cigarette smoking is not the most important factor accounting for the difference, because the frequency of lung cancer did not show a parallel distribution. The author concluded that the incidence of malnutrition and infection among immigrants from Asia and Africa is a more important factor in contributing to the higher incidence of lung disease.

BIBLIOGRAPHY

IV. PULMONARY EMPHYSEMA-BRONCHITIS COMPLEX

B. MORTALITY STATISTICS IN FOREIGN COUNTRIES

Reprint

ANDERSON D O: Observations on the classification and distribution of pulmonary emphysema in Canada. Can Med Ass J 89: 709-16, 1963. 306

ANDERSON D O: Geographic variation in deaths due to emphysema and bronchitis in Canada. Can Med Ass J 98: 231-41, 1968. 307

BEST E W R, WALKER C B, BAKER P M, DELAQUIS F M, McGREGOR J T and McKENZIE A C: Summary of a Canadian study of smoking and health. Can Med Ass J 96: 1104-8, 1967. 308

CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE: Trends in death rates for diseases of interest in relation to smoking, Canada 1950 to 1964. 1966a 309

CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE: A Canadian study of smoking and health pp 1-7, 1966b 310

CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE: A Canadian study of smoking and health. pp 41-50, 1966c 311

COHEN J: Chronic bronchitis and emphysema. Observations on trends and distribution according to death certificate data, Israel 1960 to 1964. Israel J Med Sci 3: 885-89, 1967. 312

DOLL R and HILL A B: Mortality in relation to smoking: ten years' observations of British doctors. Br Med J 1: 1399-1410, 1964A. 313

DOLL R and HILL A B: Mortality in relation to smoking: ten years' observations of British doctors. Br Med J 1: 1460-67, 1964B. 314

REID D D and FLETCHER C M: International studies in chronic respiratory disease. Br Med Bull 27: 59-68, 1971. 315

IV-C. CRITIQUE OF MORTALITY STATISTICS

There are four considerations in accepting the mortality statistics of chronic lung disease to support the thesis that cigarette smoking is one of the important causes of pulmonary emphysema, and chronic bronchitis. They are as follows:

1. Sources of error in filing death certificate. The determination of the cause of death is based on the opinion of the physician signing the certificate. The postmortem examination and the clinical picture would establish the diagnosis of pulmonary emphysema or chronic bronchitis. However, the majority of the certificates state the cause of death on the basis of symptomatology, which may not necessarily identify the cause of death. The increase in mortality is dependent to a great extent upon more frequent diagnosis based on incomplete pulmonary function tests and symptomatology rather than upon a true increase in incidence (Barach, 1964; Barach and Segal, 1968; Barach, 1971). For pulmonary emphysema Rosenblatt (1970, 1972) explained the increase in mortality to be an artifact produced by revision of the International List of Causes of Death in 1949, permitting emphysema to be accepted as a primary cause of death. The widespread publicity given to emphysema in scientific and popular publications and the Social Security compensation for disability from emphysema contribute to the record of the sudden increase of deaths from this disease.

2, Influence of air pollution on mortality statistics. The mortality statistics for the entire United States have been handled in their entirety,

ignoring important regional differences. There are differences in death rates from pulmonary emphysema and chronic bronchitis which relate to socioeconomic classes, provided that concentrations of air pollutants remain constant (Zeidberg et al., 1967). Comparison of mortality statistics in selected areas of the United States with differences in the level of air pollution reveal that environmental pollutants are important in influencing the death rate (Winkelstein et al., 1967; Buell et al., 1967; Hickey et al., 1967). In Great Britain the incidence of mortality rate from chronic bronchitis is correlated significantly with the level of air pollution (Fry, 1954; Pemberton and Goldberg, 1954; Reid, 1956; Crofton, 1965).

3. Factors influencing prognosis of chronic bronchitis and pulmonary emphysema. The most widely known factor that influences the prognosis of a patient with chronic pulmonary disease is cigarette smoking. There are other factors that are equally important and even more so, such as age, sex, geographical altitude, occurrence of cardiac complications, and extent of respiratory insufficiency (Burrows and Earle, 1964; Mitchell et al., 1964; Renzetti et al., 1966; Sukumalchantra et al., 1966; Renzetti, 1967; Tanner, 1967; Asmundsson and Kilburn, 1969; Davis and McClement 1969; Markush, 1969). The role of each of these factors in determining the longevity of patients with chronic pulmonary disease has been determined, but their importance relative to cigarette smoking is not known.

4. Inherent characteristics of cigarette smokers. It has been stated in Section II that smokers may have genetic factors which account for the higher incidence of pulmonary emphysema as compared with nonsmokers.

Although some have been identified, others have not. In a recent study the low incidence of pulmonary emphysema among Seventh Day Adventists, has been explained largely by the fact that they are nonsmokers (Dysinger and Lemon, 1963; Lemon and Walden, 1966). The possibility that members of the families of this religious order may have inherited a trait that renders them resistant to pulmonary disease has not been excluded. The mortality encountered in alcoholics has been reported to be associated with a high incidence of smoking (Rankin et al., 1969). Excessive drinkers are usually heavy smokers (Bailey et al., 1969). Although there are known common causes of death in the alcoholic, chronic pulmonary disease is not one of them. Opium smokers develop chronic obstruction (Da Costa et al., 1971, 1972). The extent of alcoholism and drug abuse has not been considered in the case of smokers dying of chronic pulmonary disease.

BIBLIOGRAPHY

IV. PULMONARY EMPHYSEMA-BRONCHITIS COMPLEX

C. CRITIQUE OF MORTALITY STATISTICS

	Reprint
ASMUNDSSON T and KILBURN K H: Survival of acute respiratory failure. A study of 239 episodes. Ann Intern Med 70: 471-85, 1969.	316
BAILEY M B, HABERMAN P W and SHEINBERG J: Identifying alcoholics in population surveys. Millbank Mem Fund Quart 47: 235-49, 1969.	317
BARACH A L: Pulmonary emphysema: Pathogenesis and the illusion of increased incidence. Med Counterpoint 3: 40-43, 1971.	318
BARACH A L: Physical exercise in breathless subjects with pulmonary emphysema, including a discussion of cigarette smoking. Dis Chest 45: 113-28, 1964.	319
BARACH A L and SEGAL M S: The increased recognition and incidence of chronic bronchitis and pulmonary emphysema. Ann Allergy 26: 353-57, 1968.	320
BUELL P, DUNN J E and BRESLOW L: Cancer of the lung and Los-Angeles-type air pollution. Cancer 20: 2139-47, 1967.	321
BURROWS B and EARLE R H: Course and prognosis of chronic obstructive lung disease. N Engl J Med 280: 397-404, 1964.	322
CROFTON E C: A comparison of the mortality from bronchitis in Scotland and in England and Wales. Br Med J 1: 1635-39, 1965.	323
DA COSTA J L, TOCK E P C and BOEY H K: Lung disease with chronic obstruction in opium smokers in Singapore. Thorax 26: 555-71, 1971.	324
DYSINGER P W and LEMON F R: Pulmonary emphysema in a non-smoking population. Dis Chest 43: 17-25, 1963.	325
DA COSTA J L, TOCK E P C and BOEY H K: Chronic obstructive lung disease in Singapore. Am Rev Resp Dis 106: 246-59, 1972.	326
DAVIS A L and McCLEMENT J H: The course and prognosis of chronic obstructive pulmonary disease. Pub Health Serv Pub 1879: 219-34, 1969.	327
FRY J: Chronic bronchitis in general practice. Br Med J 1: 190-94, 1954.	328
HICKEY R J, SCHOFF E P and CLELLAND R C: Relationship between air pollution and certain chronic disease death rates. Arch Environ Health 15: 728-38, 1967.	329
LEMON F R and WALDEN R T: Death from respiratory system disease among seventh-day adventist men. JAMA 198: 137-46, 1966.	330
MARKUSH R E: National chronic respiratory disease mortality study. II Mortality associated with persistent cough and phlegm in the United States, 1963. J Chronic Dis 21: 737-48, 1969.	331
MITCHELL R S, WEBB N C and FILLEY G F: Chronic obstructive bronchopulmonary disease. III Factors influencing prognosis. Am Rev Resp Dis 89: 878-96, 1964.	332
PEMBERTON J and GOLDBERG C: Air pollution and bronchitis. Br Med J 2: 567-70, 1954.	333

RANKIN J G, HALE G S, WILKINSON P, O'DAY D M, SANTAMARIA J N and BABARCZY G: Relationship between smoking and pulmonary disease in alcoholism. Med J Australia 1: 730-33, 1969. 334

REID DD: Symposium: Chronic bronchitis. Proc Royal Soc Med 49: 767-71, 1956. 335

RENZETTI A D Jr: Prognosis in chronic obstructive pulmonary disease. Med Clin NAm 51: 363-71, 1967. 336

RENZETTI A D Jr, McCLEMENT J H and LITT B D: The Veterans administration cooperative study of pulmonary function. Mortality in relation to respiratory function in chronic obstructive pulmonary disease. Am J Med 41: 115-29, 1966. 337

ROSENBLATT M B: Validity of emphysema mortality data. Rev Allergy 24: 1019-22, 1970. 338

ROSENBLATT M B: Emphysema: historical perspective. Bull N Y Acad Med 48: 823-41, 1972. 339

SUKUMALCHANGRA Y, DINAKARA P and WILLIAMS M H Jr: Prognosis of patients with chronic obstructive pulmonary disease after hospitalization for actue ventilatory failure: A three-year follow-up study. Am Rev Resp Dis 93: 215-22, 1966. 340

TANNER E: The prognosis of respiratory diseases. Proc 9th int Congr Life Ass Med 330-43, 1967. 341

WILKELSTEIN W Jr, KANTOR S, DAVIS E W, MANERI C S, and MOSHER W E: The relationship of air pollution and economic status to total mortality and selected respiratory system mortality in man. Arch Environ Health 14: 162-71, 1967. 342

ZEIDBERG L D, HORTON R J M and LANDAU E: Mortality from diseases of the respiratory system in relation to air pollution. Arch Environ Health 15: 214-24, 1967. 343

V. NON-OCCURRENCE OF CHRONIC PULMONARY DISEASE IN SMOKERS

The morbidity statistics are derived from the analysis of a questionnaire on the occurrence of respiratory symptoms or from examination of individuals who undergo a simple test of ventilatory function. All these surveys show a high incidence of respiratory symptoms and subnormal ventilatory function in smokers as compared with nonsmokers. This is one basis for concluding that cigarette smoking is one of the important causes of chronic obstructive pulmonary disease, also referred to in the preceding section as the pulmonary emphysema-chronic bronchitis complex.

It should be emphasized that the prevalence of respiratory symptoms among smokers ranges from 10 to 40% in various surveys, and that 60 to 90% of smokers do not complain of coughing, expectoration or shortness of breath. Those that do complain do not necessarily suffer from chronic bronchitis or pulmonary emphysema because these symptoms are also characteristic of other chronic pulmonary diseases, such as bronchial asthma, pulmonary tuberculosis and other specific forms of infection of the lung. In the absence of such diseases, the symptoms may originate from exposure to industrial hazards. Inhalation of dust particles and of pollutants has been ignored in attempts to relate cigarette smoking to respiratory symptoms. The following bibliographic lists are appended containing articles relating to morbidity studies and industrial hazards in general:

No. 11. Morbidity studies.

No. 12. Industrial hazards.

V-A. SPECIFIC FORMS OF PULMONARY DISEASE

Pulmonary emphysema and chronic bronchitis as separate diseases are discussed in Sections II and III respectively. The other forms of chronic pulmonary disease which have been investigated in smokers are discussed in this section. The monograph by Mork (1962), dealing with a comparative study of respiratory disease in England, Wales and Norway, summarizes the literature on the role of smoking in causing chronic pulmonary disease.

1. Pulmonary tuberculosis. In England, mortality from pulmonary tuberculosis in middle and later life is higher for males than for females. Lowe (1956) noted a higher proportion of smokers among tuberculous patients than among nontuberculous controls and concluded that smoking is an important cause of the breakdown of healed or quiescent respiratory tuberculosis in adults. Confirmation of the association has been reported by Edwards (1957) in England, by Shah et al. (1959) and Viswanathan et al. (1965) in India, by Nakajima (1966) in Japan, by Lawther (1966) in the Netherlands, by Adelstein and Rimington (1967) in England, and by Sussmann (1967) in Germany. Snider et al. (1971) reviewed 4,092 patients discharged from a tuberculosis sanitarium in Chicago and found no correlation between cigarette smoking and chronic airway obstruction. There is a high incidence of emphysema in tuberculous patients but a cause and effect relationship has not been established (Lancaster and Tomashefski, 1963; Katz and Yanofsky, 1964; Geiser and Steinmann, 1969).

2. Pulmonary fibrosis. This rare disease has been examined for its occurrence among smokers and nonsmokers. Cullen et al. (1965) reported two nonsmokers in a group of 12 patients from New York. Weiss (1967, 1969) listed six nonsmokers in a group of 31 patients from Pennsylvania. Among 100 asbestos textile workers in Pennsylvania six nonsmokers were included among the 35 patients diagnosed as having pulmonary fibrosis (Weiss, 1971). A high incidence of smokers has been reported among patients with pulmonary fibrosis in Guyana (Miller et al., 1968, 1971) and Rumania (Lupu et al., 1966).

3. Bronchial asthma and allergy to tobacco. A few asthmatic patients have been reported in the literature who are allergic to tobacco (Jimenez-Diaz and Cuenza, 1935; Rosen, 1946; Rosen and Levy, 1950; Segal and Dulfano, 1965; Blue, 1970). Skin tests against tobacco extract are usually positive in smokers regardless of whether asthma is present or absent (Pavlik and Cermakova, 1964). The presence of anti-tobacco precipitins has been reported in over half of those who smoke (Aiache et al., 1972). The significance of these observations has not been elucidated. The coexistence of bronchial asthma and pulmonary emphysema has been demonstrated but this does not imply that the former is a cause of the latter (Lowell, 1959; Winkenwerder et al., 1962; Rowe and Rowe, 1965; Horowitz, 1969; Preiser et al., 1969).

4. Other diseases. Spontaneous pneumothorax occurs in smokers. Legrand et al. (1971) postulated that smoking is the cause of the disease, where Zivy (1970), Zivy and Fournier (1970) and Berard and Emonot (1972) discount it. In a survey of 185 patients with pulmonary chickenpox in Australia,

smoking was a highly significant associated factor (Knyvett, 1967). There is a high incidence of peptic ulcer (about 25%) in patients with pulmonary emphysema. Although a majority of these patients are smokers, it is not possible to state that smoking is the cause of these ulcers (Lowell et al., 1956; Kroeker and Leon, 1962). Other factors, such as vagotonia, hypercapnia, hypoxia and genetic factors should be considered.

V. NON-OCCURRENCE OF CHRONIC PULMONARY DISEASE IN SMOKERS

A. SPECIFIC FORMS OF PULMONARY DISEASE

Reprint

ADELSTEIN A M and RIMINGTON J: Smoking and pulmonary tuberculosis an analysis based on a study of volunteers for mass miniature radiography. Tubercle 48: 219-226, 1967. 344

AIACHE J M, CHEMINAT J C; LAKATOS M and MOLINA C: Precipitines anti-tabac et affections des voies respiratoires. Rev de Tuberculose et Pneumologie 36: 301-7, 1972. 345

BERARD J and EMONOT A: Enquete sur l'etiologie du pneumothorax spontane dit idiopathique. (Investigation on the etiology of so-called 'idiopathic' spontaneous pneumothorax.) J Med Lyon 1223: 281-90, 1972. 346

BLUE J A: Cigarette asthma and tobacco allergy. Ann Allergy 28: 110-15, 1970. 347

CULLEN J H, KATZ H L and KAEMMERLEN J T: Chronic diffuse pulmonary infiltration and airway obstruction. Am Rev Resp Dis 92: 775-80, 1965. 348

D'ANELLI A, PROSCIA N, SORISIO F, and CARATTI C A: L'enfisema polmonare cronico ostruttivo nel malato ulceroso. Arch Sci Med 125: 191-94, 1968. 349

EDWARDS J H: Contribution of cigarette smoking to respiratory disease. Br J Prev Soc Med 11: 10-21, 1957. 350

GEISER V B and STEINMANN B: Infektionen im alter. Z Gerontologie 2: 69-85, 1969. 351

HOROWITZ L: Chronic obstructive bronchopulmonary disease (emphysema?) in children with asthma. J Asthma Res 6: 211-17, 1969. 352

JIMINEZ-DIAZ C and CUENZE B S: Asthma produced by susceptibility to unusual allergens. J Allergy 6: 397-403, 1935. 353

KATZ J and KUNOFSKY: Tuberculosis as a cause of the increasing mortality from emphysema. Am Rev Resp Dis 89: 673-79, 1964. 354

KNYVETT A F: The relation between tobacco smoking and pulmonary chickenpox. Med J Aust 2: 1197-98, 1967. 355

KROEKER E J and LEON A S: The association of diffuse obstructive pulmonary emphysema and chronic gastroduodenal ulceration. Dis Chest 42: 413-21, 1962. 356

LANCASTER J F and TOMASHEFSKI J F: Tuberculosis -- a cause of emphysema. Am Rev Resp Dis 87: 435-37, 1963. 357

LAWTHER P J. Air pollution and respiratory disease. Ned Tijds Genees 110: 2318-19, 1966. 358

LEGRAND M, BOTTO M J and LESOBRE R: Le pneumothoraz spontane. Recherches etiologiques suggerees par la prevalence masculine de l'affection. (The spontaneous pneumothorax. Etiologic investigation suggested by the prevalence of the disease in the male subjects). Le Poumon et le Coeur 27: 827-43, 1971. 359

LOWE C R: An association between smoking and respiratory tuberculosis. Br Med J 2: 1081-86, 1956. 360

LOWELL F C: The relationship of allergy to emphysema. Am Rev Resp Dis 80: 181-83, 1959. 361

LOWELL F C, FRANKLIN W, MICHELSON A L, and SCHILLER I W: A note on the association of emphysema, peptic ulcer and smoking. N Engl J Med 254: 123-24, 1956. 362

LUPU D N G, VELICAN C and RACOVEANU C: Fibrosis pulmonar por tabaco. Prensa Med Argent 53: 646-51, 1966. 363

MILLER G J, ASHCROFT M T, BEADNELL H M S G, WAGNER J C and PEPYS J: The lipoid pneumonia of blackfat tobacco smokers in Guyana. Quart J Med 15: 457-70, 1971. 364

MILLER G J, BREADNELL H M S G and ASHCROFT M T: Diffuse pulmonary fibrosis and blackfat-tobacco smoking in Guyana. Lancet 2: 259-60, 1968. 365

MORK T: A comparative study of respiratory disease in England and Wales and Norway. Acta Med Scand 172 (Suppl 384): 1-100, 1962. 366

NAKAJIMA T: A study on chronic bronchitis complicated with pulmonary tuberculous patients. Kekkahu 41: 337-44, 1966. 367

PAVLIK I and CERMAKOVA Z: Casna kozni reakce na tabakovy extrakt u chorob dychadel. (Early skin reactions against tobacco extract in respiratory system disease). Rozhledy Tuberk Nem Plicnik 24: 629-35, 1964. 368

PREISER F M, DONNER M W and VAN METRE T E Jr: Comparison of midplane, full-chest tomograms, duffusing capacities, sputum eosinophil content, and other parameters in patients with asthma and emphysema. J Allergy 44: 154-64, 1969. 369

ROSEN F L: Bronchial asthma in the young male adult. Ann Allergy 4: 247-60, 1946. 370

ROSEN F L and LEVY A: Bronchial asthma due to allergy to tobacco smoke in an infant. JAMA 144: 620-21, 1950. 371

ROWE A H and ROWE A Jr: Food allergy -- its role in emphysema and chronic bronchitis. Dis Chest 48: 609-12, 1965. 372

SEGAL M S and DULFANO M J: Glomectomy in the treatment of chronic bronchial asthma. N Engl J Med 272: 57-63, 1965. 373

SHAH J R, WARAWADEKAR M S, DESHMUKH P A and PHUTANE P N: Institutional survey of pulmonary tuberculosis with special reference to smoking habits. Indian J Med Sci 13: 381-92, 1959. 374

SNIDER G L, DOCTOR L, DEMAS T A and SHAW A E: Obstructive airway disease in patients with treated pulmonary tuberculosis. Am Rev Resp Dis 103: 625-40, 1971. 375

SUSSMANN F H A: Die chronischen unspezifischen lungenerkrankungen aus der sicht des kreistuberkulosearztes. Z Tuberk 127: 191-202, 1967. 376

VISWANATHAN R, MODY R K, PRASAD S S and SINHA S P: Bronchial asthma and chronic bronchitis. J Indian Med Assoc 45: 480-83, 1965. 377

WEISS W: Cigarette smoking and diffuse pulmonary fibrosis. Arch Environ Health 14: 564-68, 1967. 378

WEISS W: Cigarette smoking and diffuse pulmonary fibrosis. Am Rev Resp Dis 99: 67-72, 1969. 379

WEISS W: Cigarette smoking, asbestos, and pulmonary fibrosis. Am Rev Resp Dis 104: 223-27, 1971. 380

WINKENWERDER W L, ALLAN W B and FISHER A M: A consideration of the etiology of obstructive emphysema, with especial emphasis on the role of allergy. Trans Am Clin Climatol Assoc 74: 1-14, 1962. 381

ZIVY P: Le pneumothorax spontane des fumeurs. Le poumon tabagique. Rev Tuberc Pneumol 34: 125-58, 1970. 382

ZIVY P and FOURNIER E: Tabagisme, emphyseme bulleux et pneumothorax spontane (P. S. I.) idiopathique. Ann Med Intern 121: 1049-56, 1970. 383

V-B. MORBIDITY STATISTICS IN THE UNITED STATES

The prevalence of respiratory symptoms among cigarette smokers has been investigated in several states. Some of the surveys consider the additional role of industrial hazards and of air pollution in the causation of symptoms which suggest the presence of chronic pulmonary disease.

1. New Hampshire. In 1961, a study of prevalence of respiratory disease among 1,261 residents of Berlin, New Hampshire, was carried out (Ferris and Anderson, 1965; Anderson and Ferris, 1962; Anderson et al., 1963). It was observed that in cigarette smokers, chronic respiratory disease was substantially more prevalent than in nonsmokers of similar age and sex. A repeat study of the group in 1967 showed a lower prevalence of such disease than in 1961. The levels of air pollution were less in the second study than in the first, and it was suggested that this fall accounted for the decrease in prevalence of the disease and improvement in lung function (Ferris et al., 1971). Eckardt (1972) and Ferris et al., (1973) have exchanged correspondence with each other on the results that pulmonary function is better in males smoking 45 cigarettes /day than in those who smoke 1 to 4 cigarettes.

The above studies emphasize the shortcomings of morbidity statistics which attempt to correlate cigarette smoking with incidence of respiratory disease. If cigarette smoking is indeed an important cause of lung disease, continued smoking from 1961 to 1967 would have increased its incidence, but this did not occur. The effects of the reduction in air pollution appear to show that atmospheric impurity is a more important

cause of lung disease than cigarette smoking. A group of 147 men drawn from workers in a pulp mill was compared with one of 124 men from a paper mill. Although the pulp mill workers were exposed to chlorine and sulfur dioxide, there was no significant difference between the two groups in regard to respiratory symptoms and ventilatory function. The working population of both mills together showed a lower prevalence of respiratory disease than did the male population of Berlin, N. H., suggesting that the working population may not be representative of the general population (Ferris et al., 1967).

2. Massachusetts. A sample of the population of Framingham has been examined periodically for symptoms of lung disease., chest x-ray and ventilatory function (Revotskie et al., 1962). The results do not show any correlation between smoking and incidence of symptoms or reduction in ventilatory function. The following groups were found to show a higher incidence of respiratory symptoms among smokers than nonsmokers: 5,000 registrants for military service (Andosca, 1966); 100 college seniors and (Peters and Ferris, 1967); 2,027 university graduates (Peters and Ferris, 1967). In the second group there was no statistically significant difference in vital capacity and forced expiratory volume between smokers and nonsmokers. In the third group, the higher incidence of respiratory symptoms in addition was accompanied by traumatic and genitourinary problems. The authors do not attribute the high incidence of trauma and genitourinary problems among smokers to cigarette smoking, yet they

ascribe the respiratory symptoms to it.

Two groups of workers were surveyed in Massachusetts. Ferris et al. (1968) examined movie projectionists and noted no difference in ventilatory function between smokers and nonsmokers.

3. Connecticut. A group of 424 persons residing in Southern Connecticut were questioned for incidence of respiratory symptoms (Kelsey et al., 1968). Smokers were affected more frequently than nonsmokers. However, a statistically significant association was observed between severity of symptoms and migration from urban areas. The chronic bronchitics with severe symptoms were most likely to have left urban areas afflicted with air pollution in recent years.

A retrospective study was made of medical absenteeism among 226 male employees of a manufacturing company from 1956 through 1964 (Holcomb and Meigs, 1972). There was a significant association of high absenteeism with cigarette smoking and a more significant association of low absenteeism with cigar or pipe smoking. The authors proposed a hypothesis that adoption of the habit of cigar or pipe smoking at middle age occurred among men with constitutional and absentee behavioral characteristics tending to distinguish them from men with a lifelong cigarette smoking habit. The authors suggested caution in drawing causal conclusions regarding these associations because of considerable overlapping of individual absentee rates among groups divided by smoking habits.

4. New York. The following groups solicited by a questionnaire show a higher incidence of respiratory symptoms among smokers than among nonsmokers: 2,031 insurance policy holders (Short et al., 1939); 1,250 telephone men over 40 years of age (Holland and Stone, 1965; Comstock et al., 1970); and 12,604 postal and transit workers (Densen et al., 1967). In the last-mentioned study, there was a decrease of forced expiratory volume with age, particularly among white men more than among nonwhite men (Densen et al., 1964, 1967). A similar racial difference was encountered in a survey of 6,314 workers for pulmonary emphysema (Robins et al., 1969).

Two surveys were made of industrial workers. A group of 55 grain handlers in Western New York State (Kleinfeld et al., 1968). There was no significant difference in vital capacity between smokers and nonsmokers up to 19 years of age but a significant difference in vital capacity and forced expiratory volume between these two types of subject when 20 years old or more. A group of 1,744 individuals exposed to oil mist showed a higher incidence of respiratory symptoms for smokers than for nonsmokers (Ely et al., 1970).

5. Pennsylvania. Boucot et al. (1962) reported that among 6,137 males over 45 years of age there was a higher incidence of chronic cough among smokers than among nonsmokers. A similarity in cough pattern appeared in cigarette, cigar and pipe smokers,

suggesting that tobacco smoke in general rather than cigarette smoke alone causes cough.

The other reports from Pennsylvania concern coal miners. In a group of 801 anthracite coal miners, smoking, aging and duration of exposure to coal dust increased the prevalence of pneumoconiosis (Tokuhata et al., 1970). Autopsies performed on a group of 144 Appalachian underground coal workers indicated no significant effect of smoking on lung structure in anthracite miners (Naeye et al., 1971). Among bituminous coal miners, the smokers had a greater degree of cor pulmonale and more emphysema and bronchiolar goblet cells. The authors suggested that the effect of smoking among anthracite miners may be obscured by the severe lesions primarily related to the pneumoconiosis. Another possibility is that above-ground forms of air pollution may partially obscure the influence of smoking. In response to a communication from Kibelstis (1972), the authors emphasized that it is not yet possible to quantitate the individual contributions to emphysema of mine dust, smoking, other air pollutants, infection and other factors of individual susceptibility.

6. West Virginia. The data collected from 258 bituminous miners show a higher incidence of respiratory symptoms among smokers than among nonsmokers (Hyatt et al., 1964). In another survey of 5,540 persons living in five communities, there was a higher incidence of respiratory symptoms among smokers than among nonsmokers (Higgins et al., 1968). The mean of forced expiratory volume of smokers and that of nonsmokers under 50 years of age were not different but these were lower for smokers and nonsmokers

over 50 years of age.

That chronic obstructive disease can still occur among miners who are nonsmokers indicates the importance of exposure to coal dust as a causative factor (Rasmussen, 1971; Rasmussen and Nelson, 1971). The reduction in the ventilatory function of coal miners who are smokers is particularly marked after the end of the working period (Lapp et al., 1972). The prevalence of respiratory symptoms in a mining community is the same both for miners and for nonminers, so that the contamination of the air influences the incidence of lung disease (Enterline and Lainhart, 1967).

7. Maryland. Stebbings (1971 a, b, c, d) has reported the results of examination of 736 white males, 35 to 64 years old, who were nonsmokers. Although the investigation did not include smokers, several problems relating to statistics became apparent. The prevalence of respiratory symptoms or illness as derived from the standard questionnaire does not discriminate adequately between upper respiratory allergic conditions, lower respiratory symptoms and cardiovascular symptoms. The pulmonary function values included sizable instrument and interviewer data that were statistically significant. Social class can influence respiratory symptoms and pulmonary function. Furthermore, the effect of duration of urban residence on pulmonary function vary. Most of the shortcomings uncovered by Stebbings were overlooked in prevalence studies reported by the United States Public Health Service.

8. Southern States. The incidence of respiratory symptoms among smokers is higher than among nonsmokers in the foll owing groups: 1, 848 military cadets in Georgia (Finklea et al., 1971), and 408 cotton textile workers in North Carolina (Merchant et al., 1972) and in Georgia (Bouhuys et al., 1969). In Tennessee, the extent of air pollution has been shown to influence the incidence of respiratory symptoms (Zeidberg et al., 1964).

9. Michigan. In 1958 a group of 1, 317 men, ranging in age from 40 to 65 years, with industrial exposure in the Detroit area, were examined (Brinkman and Coates, 1962). Cigarette smoking was identified as the most important factor in the etiology of chronic bronchitis diagnosed by the occurrence of expectoration daily for at least six months. After a six-year period, the subjects diagnosed as chronic bronchitics did not show any adverse effect on health, working ability or ventilation even though they continued smoking (Brinkman and Block, 1966, 1972).

Additional surveys have appeared relating to the following: 6,500 residents of Tecumseh (Payne and Kjelsberg, 1964; Higgins and Kjelsberg, 1967); 1,584 Detroit postal employees 40 years of age or older (Coates et al., 1965); and 1, 058 iron foundry workers (Clarke, 1972). A higher incidence of respiratory symptoms among smokers than among nonsmokers was reported.

10. Minnesota. In a group of 450 railroad employees, there was a correlation between intensity of smoking and the expiratory volumes and incidence of symptoms (Blackburn et al., 1965). In subjects who stopped smoking, the ventilatory function was elevated to "supernormal" level. The authors have interpreted this as strengthening the concept that smokers differ from nonsmokers in characteristics other than the smoking habit.

11. Midwestern states. The following surveys have revealed a higher incidence of respiratory symptoms among smokers than among nonsmokers: 1,887 white males 43 to 58 years old employed in an industrial plant in Illinois (Sharp et al., 1965); 136 white-collar workers 35 to 64 years of age in Ohio (Krumholz and Hedrick, 1973); 557 high school students in Oklahoma.(Addington et al, 1970).

12. Colorado. In a group of 172 adult men and women over 40 years of age, ventilatory function in male nonsmokers was significantly better than in smokers, but there was no significant difference between female nonsmokers and smokers (Bower, 1961). In a prevalence study of 633 residents of Glenwood Springs, a strong association was found to exist between incidence of chronic bronchitis and cigarette smoking (Mueller et al., 1971 a, b). The authors reviewed interstudy variations in the prevalence of respiratory disease in various geographic areas and concluded that there are other factors which determine the incidence of chronic

obstructive pulmonary disease. In a group of 1,500 uranium miners, cigarette smoking did not influence the occurrence of shortness of breath or persistent coughing (Archer et al., 1964). The hazards of radiation exposure are more severe than other factors, such as aging, altitude and cigarette smoking.

12. California. The following surveys indicate a higher incidence of respiratory symptoms among smokers than among nonsmokers: 7,070 industrial workers in Los Angeles County (Balchum et al., 1962); 3,311 longshoremen in San Francisco bay area (Goldsmith et al., 1962); and 630 telephone workers in San Francisco and Los Angeles (Deane et al., 1965). In a group of 38 beryllium workers, ventilatory function was measured at 6-month intervals for 18 to 24 months. The day-to-day variation in values was greater for smokers than for nonsmokers (Dawson, 1966).

BIBLIOGRAPHY

V. NON-OCCURRENCE OF CHRONIC PULMONARY DISEASE IN SMOKERS

B. MORBIDITY STATISTICS IN THE UNITED STATES

Reprint

ADDINGTON W W, CARPENTER R L, DUNCAN K A and MOGG K: The Association of Cigarette Smoking With Respiratory Symptoms and Pulmonary Function in a Group of High School Students. Oklahoma Med Ass J 63: 525-29, 1970. 384

ANDERSON D O and FERRIS B G Jr: Role of Tobacco Smoking in the Causation of Chronic Respiratory Disease. N Engl J Med 267: 787-94, 1962. 385

ANDERSON D O, ZICKMANTEL R and FERRIS B G Jr: Response to a Respiratory Survey. Canad Med Ass J 88: 596-602, 1963. 386

ANDOSCA J B: The Incidence of Smoking and the Smoking Habits in 5000 Registrants for Military Service. J Am Geriatr Soc 14: 631-32, 1966. 387

ARCHER V E, CARROL B E, BRINTON H P, and SACCOMANNO G: Epidemiological Studies of some Non-fatal Effects of Uranium Mining. In: Radiological Health and Safety in Mining and Milling of Nuclear Materials, Vol I, International Atomic Energy Agency: Vienna 21-36, 1964. 388

BALCHUM O J, FELTON J S, JAMISON J N, GAINES R S, CLARKE D R and OWAN T: A Survey for Chronic Respiratory Disease in an Industrial City. Am Rev Resp Dis 86: 675-85, 1962. 389

BLACKBURN H, TAYLOR H L, PARLIN R W, KIHLBERG J and KEYS A: Physical Activity of Occupation and Cigarette Smoking. Arch Environ Health 10: 312-22, 1965. 390

BOUCOT K R, COOPER D A and WEISS W: Smoking and the Health of Older Men. Arch Environ Health 4: 59-72, 1962. 391

BOUHUYS A, WOLFSON R L, HORNER D W, BRAIN J D and ZUSKIN E: Byssinosis in Cotton Textile Workers. Respiratory Survey of a Mill with Rapid Labor Turnover. Ann Intern Med 71: 257-69, 1969. 392

BOWER G: Respiratory Symptoms and Ventilatory Function in 172 Adults Employed in a Bank. Am Rev Resp Dis 83: 684-89, 1961. 393

BRINKMAN G L and BLOCK D L: The Prognosis in Chronic Bronchitis. JAMA 197: 71-77, 1966. 394

BRINKMAN G L and BLOCK D L: Chronic bronchitis in a Working Population. J Occup Med 14: 825-27, 1972. 395

BRINKMAN G L and COATES E O: The Prevalence of Chronic Bronchitis in an Industrial Population. Am Rev Resp Dis 86: 47-54, 1962. 396

CLARKE N E Sr.: Silicosis and Diseases of Retired Iron Foundry Workers. Ind Med 41: 22-25, 1972. 397

COATES E O Jr, BOWER G C and Reinstein N: Chronic Respiratory Disease in Postal Employees. JAMA 191: 161-66, 1965. 398

COMSTOCK G W, BROWNLOW W J, STONE R W and SARTWELL P E: Cigarette Smoking and Changes in Respiratory Findings. Arch Environ Health 21: 50-59, 1970. 399

DAWSON A: Reproducibility of Spirometric Measurements in Normal Subjects. Am Rev Resp Dis 93: 264-268, 1966. 400

DEANE M, GOLDSMITH J R and TUMA D: Respiratory Conditions in Outside Workers. Arch Environ Health 10: 323-331, 1965. 401

DENSEN P M, JONES E W, BASS H E and BREUER J: A Survey of Respiratory Disease Among New York City Postal and Transit Workers. Environ Res 1: 262-86, 1967. 402

DENSEN P M, JONES E W, BASS H E, BREUER J and REED E: A Survey of Respiratory Disease Among New York City Postal and Transit Workers. Environ Res 2: 277-96, 1964. 403

ECKARDT R E: Chronic Nonspecific Respiratory Disease, Berlin, New Hampshire 1961-1967: A Cross Section Study. Am Rev Resp Dis 105: 854, 1972. 404

ELY T S, PEDLEY S F, HEARNE F T and STILLE W T: A study of mortality, symptoms, and respiratory function in humans occupationally exposed to oil mist. J Occup Med 12: 253-61, 1970. 405

ENTERLINE P E and LAINHART W S: The relationship between coal mining and chronic nonspecific respiratory disease. Am J Public Health 57: 484-95, 1967. 406

FERRIS B G and ANDERSON D O: The prevalence of chronic respiratory disease in a New Hampshire town. Am Rev Resp Dis 86: 165-77, 1965. 407

FERRIS B G Jr, BURGESS W A and WORCESTER J: Prevalence of chronic respiratory disease in a pulp mill and a paper mill in the United States. Br J Ind Med 24: 26-37, 1967. 408

FERRIS B G Jr, BURGESS W A and WORCESTER: Chronic nonspecific respiratory disease in a movie projectionists union. Arch Environ Health 16: 886-91, 1968. 409

FERRIS B G Jr, HIGGINS I T T, HIGGINS M W, PETERS J M, VAN GANSE W F and GOLDMAN M D: Chronic nonspecific respiratory disease, Berlin, New Hampshire, 1961-1967: A cross-sectional study. Am Rev Resp Dis 104: 232-44, 1971. 410

FERRIS B G Jr, HIGGINS I T T, HIGGINS M W and PETERS J M: Chronic nonspecific respiratory disease in Berlin, New Hampshire, 1961 to 1967. A follow-up study. Am Rev Resp Dis 107: 110-22, 1973. 411

FINKLEA J F, HASSELBLAD V, SANDIFER S H, HAMMER D I and LOWRIMORE G R: Cigarette smoking and acute non-influenzal respiratory disease in military cadets. Am J Epidemiol 93: 457-62, 1971. 412

GOLDSMITH J R, HECHTER H H, PERKINS N M and BORHANI N O: Pulmonary function and respiratory findings among longshoremen. Am Rev Resp Dis 86: 867-74, 1962. 413

HIGGINS I T T, HIGGINS M W, LOCKSHIN M D and CANALE N: Chronic respiratory disease in mining communities in Marion County, West Virginia. Br J Ind Med 25: 165-75, 1968. 414

HIGGINS M W and KJELSBERG M: Characteristics of smokers and nonsmokers in Tecumseh, Michigan. Am J Epidemiol, 86: 60-77, 1967. 415

HOLCOMB III H S, and MEIGS J W: Medical absenteeism among cigarette, and cigar and pipe smokers. Arch Environ Health 25: 295-300, 1972. 416

HOLLAND W W and STONE R W: Respiratory disorders in United States east coast telephone men. Am J Epidemiol 82: 92-101, 1965. 417

HYATT R E, KISTIN A D and MAHAN T K: Respiratory disease in southern West Virginia coal miners. Am Rev Resp Dis 89: 387-401, 1964. 418

KELSEY J L, MOOD E W and ACHESON R M: Population mobility and epidemiology of chronic bronchitis in Connecticut. Arch Environ Health 16: 853-61, 1968. 419

KIBELSTIS J A: Coal workers' pneumoconiosis. JAMA 221: 301-02, 1972. 420

KLEINFELD M, MESSITE J, SWENCICKI R E and SHAPIRO J: A clinical and physiologic study of grain handlers. Indust Hyg Rev 10: 12-19, 1968. 421

KRUMHOLZ R A and HENDRICK E C: Pulmonary function differences in normal smoking and nonsmoking, middleaged, white-collar workers. Am Rev Resp Dis 107: 225-30, 1973. 422

LAPP N L, HANKINSON J L, BURGESS D B and O'BRIEN R: Changes in ventilatory function in coal-miners after a work shift. Arch Environ Health 24: 204-8, 1972. 423

MERCHANT J A, KILBURN K H, O'FALLON W M, HAMILTON J D and LUMSDEN J C: Byssinosis and chronic bronchitis among cotton textile workers. Ann Intern Med 76: 423-33, 1972. 424

MUELLER R E, KEBLE D L, PLUMMER J and WALKER S H: The prevalence of chronic airway obstruction, and respiratory symptoms in a Colorado city. Am Rev Resp Dis 103: 209-28, 1971A. 425

MUELLER R E, WALKER S H and PLUMMER J: An epidemiologic study of chronic bronchitis, chronic airway obstruction and respiratory symptoms in a Colorado city. Hartford Hosp Bull 26: 261-97, 1971B. 426

NAEYE R L: Coal workers' pneumoconiosis. J Am Med Ass 222: 87, 1972. 427

NAEYE R L, MAHON J K and DELLINGER W S: Effects of smoking on lung structure of Appalachian coal workers. Arch Environ Health 22: 190-93, 1971. 428

PAYNE M and KJELSBERG M: Respiratory symptoms, lung function, and smoking habits in an adult population. Am J Public Health 54: 265-77, 1964. 429

PETERS J M and FERRIS B G Jr: Smoking, pulmonary function, and respiratory symptoms in a college-age group. Am Rev Resp Dis 95: 774-82, 1967. 430

PETERS J M and FERRIS B G Jr: Smoking and morbidity in a college-age group. Am Rev Resp Dis 95: 783-89, 1967. 431

RASMUSSEN D L: Impairment of oxygen transfer in dyspneic, nonsmoking soft coal miners. J Occup Med 13: 300-5, 1971. 432

RASMUSSEN D L and NELSON C W: Respiratory function in southern Appalachian coal miners. Am Rev Resp Dis 103: 240-48, 1971. 433

REVOTSKIE N, KANNELL W, GOLDSMITH J R and DAWBER T R: Pulmonary function in a community sample. Am Rev Resp Dis 86: 907-11, 1962. 434

ROBINS A B, EPSTEIN H H, DIAMOND P H, PLISHNER M J and FINKELSTEIN H: A project for the prevention of disability from chronic respiratory disease in working males. Am J Public Health 59: 77-85, 1969. 435

SHARP J T, PAUL O, LEPPER M H, McKEAN H, and SAXTON G A Jr: Prevalence of chronic bronchitis in an American male urban industrial population. Am Rev Resp Dis 91: 510-19, 1965. 436

SHORT J J, JOHNSON H J, and LEY H A Jr: The effects of tobacco smoking on health. J Lab Clin Med 24: 586-89, 1939. 437

STEBBINGS JH Jr: Chronic respiratory disease among nonsmokers in Hagerstown, Maryland. Design of the study and prevalence of symptoms. Environ Res 4: 146-62, 1971A. 438

STEBBINGS J H Jr: Chronic respiratory disease among nonsmokers in Hagerstown Maryland. Problems in the estimation of pulmonary function values in epidemiological surveys. Environ Res 4: 163-92, 1971B. 439

STEBBINGS J H Jr: Chronic respiratory disease among nonsmokers in Hagerstown, Maryland. Social class and chronic respiratory disease. Environ Res 4: 213-32, 1971C. 440

STEBBINGS J H Jr: Chronic respiratory disease among nonsmokers in Hagerstown, Maryland. Effects of urban residence on pulmonary function values. Environ Res 4: 283-304, 1971D. 441

TOKUHATA G K, DESSAUER P, PENDERGRASS E P, HARTMAN T, DIGON E, and MILLER W: Pneumoconiosis among anthracite coal miners in Pennsylvania. Am J Public Health 60: 441-51, 1970. 442

ZEIDBERG L D, PRINDLE R A and LANDAU E: The Nashville air pollution study. III: Morbidity in relation to air pollution. Am J Public Health 54: 85-97, 1964. 443

V-C. MORBIDITY STATISTICS IN GREAT BRITAIN

Chronic bronchitis is the more common form of chronic obstructive pulmonary disease in Great Britain. Fletcher (1963) and Reid et al. (1964) noted that there was little difference in the prevalence of productive cough between the United States (Berlin, New Hampshire) and all surveyed areas of Great Britain. However, the symptoms of more advanced bronchitis with infection and dyspnea were more prevalent in British areas than in the United States. Holland et al. (1965) arrived at a similar conclusion in comparing the prevalence of symptoms of advanced bronchitis in London and three American cities: Westchester (New York), Baltimore and Washington. The prevalence rates for respiratory symptoms in British male migrants are no greater than for those in native-born Americans, so that the environment is more important than country of birth (Reid et al., 1966). An Anglo-Danish comparison has revealed a higher incidence of respiratory symptoms in England than in Denmark (Olsen and Gilson, 1960).

1. Influence of air pollution. Most of the early comparisons of prevalence rates of respiratory symptoms in Great Britain involved only a single community: 1,300 subjects in London (Oswald et al., 1953); 6,245 clerical workers also in London (Oswald et al., 1955); 631 residents of an agricultural community near Penarth (Higgins et al., 1956; Higgins, 1957); 147 young soldiers at Aldershot (Liebeschuetz, 1959); 2,081 men

over 60 years of age in Birmingham (Edwards et al., 1959), and 92 general practitioners (College of General Practitioners, 1961). These surveys showed that there is a higher incidence of respiratory symptoms among smokers than nonsmokers.

Subsequent observations have emphasized the importance of air pollution in influencing the prevalence of respiratory symptoms. Higgins and Cochrane (1958) and Higgins (1959) noted a difference in incidence between a community (Annandale) in Scotland and the Vale of Glamorgan in Wales, i. e., between an urban and a rural community. The extent of influence of cigarette smoking was determined by the amount of air pollution.

The urban factor in chronic bronchitis has been studied by Holland and Reid (1965), who surveyed 293 drivers and vehicle maintenance men in central London and 477 men in three rural areas in Southern England. Although personal smoking habits were shown to be closely related to the frequency of respiratory disturbance, the local levels of air pollution appeared to be the most likely cause of the difference in morbidity between urban and rural areas. A study of 2,342 families revealed a relationship between the prevalence of cough and environmental factors. In the fathers who were exposed to the hazards both of home and of occupation, smoking and social class influenced the prevalence of cough. It was not possible to specify the role of smoking alone in incidence of coughing (Colley and Holland,

1967). Other additional surveys illustrate the importance of air pollution and of social class in influencing the incidence of symptoms of chronic bronchitis: Evans et al. (1969) at Derbyshire; Rimington (1969) at Cheshire; Howard (1970) at Sheffield; and Milne and Williamson (1972 a, b) at Edinburgh. A postal survey of 9,975 men and women in the London area, made with a questionnaire similar to that used in American surveys, revealed a difference between rural and urban areas in the incidence of respiratory symptoms (Lambert and Reid, 1970).

2. Incidence in children and young adults. Approximately 10,000 children in secondary and grammar schools completed a questionnaire relating to their smoking habits (Holland and Elliot, 1968). . . . The frequency of respiratory symptoms was higher among students who smoked more than five cigarettes a day -- about 30% coughing and 20% expectoration -- as compared with 2% and 5% among those smoking less than one cigarette a day. Holland et al. (1969 a, b, c) have summarized the analysis of their results and concluded that environmental and personal factors are important in the onset of chronic respiratory disease. Colley and Reid (1970) surveyed 10,000 children from 6 to 10 years old and noted a pronounced social class gradient in the frequency of chronic cough. The occurrence of respiratory symptoms in children is influenced by the smoking habits of the families (Norman-Taylor and Dickinson, 1972).

3. Industrial hazards. In 1957 the British Medical Research Council's Pneumoconiosis Research Unit carried out a survey in Staveley, an industrial town (Higgins et al., 1959). The prevalence of respiratory symptoms was higher and ventilatory function was lower in miners exminers and men exposed to chemical fumes than in men who had worked in nondusty jobs. After five and nine years, the follow-up study showed that the annual decline of forced expiratory volume was greater in smokers than in nonsmokers or ex-smokers (Higgins and Oldham, 1962; Higgins et al., 1968, 1969). It was concluded that smoking is a more important factor in the development of respiratory disability than occupation.

Other investigators surveying miners have not identified smoking as a more important factor than industrial hazards in the causation of respiratory symptoms (Ashford et al., 1961; Caplan et al., 1966; Ashford et al., 1970; Ryder et al., 1970; Walker et al., 1971; Lyons et al., 1972).

Among the following industrial workers, smoking contributes to the prevalence of respiratory symptoms: alkaline dust workers (Chivers, 1959), flax workers (Elwood et al., 1965), spinners (Molyneux and Tombleson, 1970), asbestos workers (Regan et al., 1971; Muldoon and Warwick ., 1972) and steel foundrymen (Lowe et al., 1970, 1972; McCallum, 1972). In the last-mentioned type of workmen, the influence of air pollution in the prevalence of respiratory symptoms has been suggested by Lowe et al. (1968).

V. NON-OCCURRENCE OF CHRONIC PULMONARY DISEASE IN SMOKERS

C. MORBIDITY STATISTICS IN GREAT BRITAIN

Reprint

ASHFORD J R, BROWN S, DUFFIELD D P, SMITH C S and FAY J W J: The relation between smoking habits and physique, respiratory symptoms, ventilatory function, and radiological pneumoconiosis amongst coal workers at three Scottish collieries. Br J Prev Soc Med 15: 106-17, 1961. 444

ASHFORD J R, MORGAN D C, RAE S and SOWDEN R R: Respiratory symptoms in British coal miners. Am Rev Resp Dis 102: 370-81, 1970. 445

CAPLAN A, SIMON G and REID L: The radiological diagnosis of widespread emphysema and categories of simple pneumoconiosis. Clin Radiol 17: 68-70, 1966. 446

CHIVERS C P: Respiratory function and disease among workers in alkaline dusts. Br J Ind Med 16: 51-60, 1959. 447

COLLEGE OF GENERAL PRACTITIONERS: Chronic bronchitis in Great Britain. Br Med J 2: 973-79, 1961. 448

COLLEY J R T and HOLLAND W W: Social and environmental factors in respiratory disease. Arch Environ Health 14: 157-61, 1967. 449

COLLEY J R T and REID D D: Urban and social origins of childhood bronchitis in England and Wales. Br Med J 2: 213-17, 1970. 450

EDWARDS F, McKEOWN T and WHITFIELD A G W: Association between smoking and disease in men over sixty. Lancet 1: 196-200, 1959. 451

ELWOOD P C, PEMBERTON J, MERRETT J D, CAREY G C R and McAULAY I R: Byssinosis and other respiratory symptoms in flax workers in Northern Ireland. Br J Ind Med 22: 27-37, 1965. 452

EVANS S M, WILKES E, and DALRYMPLE-SMITH D: Presymptomatic diagnosis. J Roy Coll Gen Practitioners 17: 237-46, 1969. 453

FLETCHER C M: An account of chronic bronchitis in Great Britain with a comparison between British and American experience of the disease. Dis Chest 44: 1-10, 1963. 454

HIGGINS I T T: Respiratory symptoms, bronchitis, and ventilatory capacity in random sample of an agricultural population. Br Med J 2: 1198-1203, 1957. 455

HIGGINS I T T: Tobacco smoking, respiratory symptoms, and ventilatory capacity. Studies in random samples of the population. Br Med J 1: 325- 29, 1959. 456

HIGGINS I T T and COCHRAN J B: Respiratory symptoms, bronchitis and disability in a random sample of an agricultural community in Dumfriesshire. Tubercule 39: 296-301, 1958. 457

HIGGINS I T T, COCHRANE A L, GILSON J C and WOOD C H: Population studies of chronic respiratory disease. A comparison of mines, foundryworkers, and others in Staveley, Derbyshire. Br J Ind Med 16: 255-68, 1959. 458

HIGGINS I T T, GILSON J C, FERRIS B G Jr, WATERS M E, CAMPBELL H and HIGGINS M W: Chronic respiratory disease in an industrial town: A nine-year follow-up study. Preliminary report. Am J Public Health 58: 1667-76, 1968. 459

HIGGINS I T T, GILSON J C, FERRIS B G, WATERS W E, CAMPBELL H, and HIGGINS M W: Chronic respiratory disease in an industrial town: A nine-year follow-up study. Respiration 26: 221-2, 1969. 460

HIGGINS I T T and OLDHAM P D: Ventilatory capacity in miners. A five-year follow-up study. Br J Ind Med 19: 65-76, 1962. 461

HIGGINS I T T, OLDHAM P D, COCHRANE A L and GILSON J C: Respiratory symptoms and pulmonary disability in an industrial town. Survey of a random sample of the population. Br Med J 2: 904-9, 1956. 462

HOLLAND W W and ELLIOTT A: Cigarette smoking, respiratory symptoms, and anti-smoking propaganda. Lancet 1: 41-43, 1968. 463

HOLLAND W W, HALIL T, BENNETT A E and ELLIOTT A: Factors influencing the onset of chronic respiratory disease. Br Med J 2: 205-8, 1969A. 464

HOLLAND W W, HALIL T, BENNETT A E and ELLIOTT A: Indications for measures to be taken in childhood to prevent chronic respiratory disease. Millbank Mem Fund Quart 47: 215-27, 1969B. 465

HOLLAND W W, HALIL T and ELLIOTT A: The effect of environmental factors on ventilatory function in schoolchildren. Pub Health Serv Pub 1879: 259-72, 1969C. 466

HOLLAND W W and REID D D: The urban factors in chronic bronchitis. Lancet 1: 445-48, 1965. 467

HOLLAND W W, REID D D, SELTSER R and STONE R W: Respiratory disease in England and the United States. Arch Environ Health 10: 338-48, 1965. 468

HOWARD P: A long-term follow-up of respiratory symptoms and ventilatory function in a group of working men. Br J Ind Med 27: 326-333, 1970. 469

LAMBERT P M and REID D D: Smoking, air pollution, and bronchitis in Britain. Lancet 1: 853- 57, 1970. 470

LEIBESCHUETZ H J: Respiratory signs and symptoms in young soldiers and their relationship to smoking. J Royal Army Med Corps 105: 76-81, 1959. 471

LOWE C R, CAMPBELL H, and KHOSLA T: Bronchitis in two integrated steel works. III. Respiratory symptoms and ventilatory capacity related to atmospheric pollution. Br J Ind Med 27: 121-29, 1970. 472

LOWE C R and KHOSLA T: Chronic bronchitis in-ex-coal miners working in the steel industry. Br J Ind Med 29: 45-49, 1972. 473

LOWE C R, PELMEAR P L, CAMPBELL H, HITCHENS R A N, KHOSLA T and KING T C: Bronchitis in two integrated steel works. I.Ventilatory capacity age and physique of non-bronchitic men. Br J Prev Soc Med 22: 1-11, 1968. 474

LYONS J P, RYDER R, CAMPBELL H and GOUGH J: Pulmonary disability in coal workers' pneumoconiosis. Br Med J 1: 713-16, 1972. 475

McCALLUM R I: Respiratory disease in foundrymen. Br J Ind Med 29: 341-44, 1972. 476

[illegible] Respiratory function tests in older people.

MILNE J S and WILLIAMSON J: The relationship of respiratory function tests to respiratory symptoms and smoking in older people. Respiration 29: 206-13, 1972B. 478

MOLYNEUX M K B and TOMBLESON J B L: An epidemiological study of respiratory symptoms in Lancashire mills, 1963-66. Br J Ind Med 27: 225-34, 1970. 479

MULDOON B C and WARWICK M T: Lung function studies in asbestos workers. Br J Dis Chest 66: 121-32, 1972. 480

NORMAN-TAYLOR W and DICKINSON V A: Dangers for children in smoking families. Community Med 128: 32-33, 1972. 481

OLSEN H C and GILSON J C: Respiratory symptoms, bronchitis and ventilatory capacity in men. An Anglo-Danish comparison, with special reference to differences in smoking habits. Br Med J 1: 450-56, 1960. 482

OSWALD N C, HAROLD J T and MARTIN W J: Clinical pattern of chronic bronchitis. Lancet 2: 639-43, 1953. 483

OSWALD N C and MEDVEI V C: Chronic bronchitis. The effect of cigarette smoking. Lancet 2: 843-44, 1955. 484

REGAN G M, TAGG B, WALFORD J and THOMSON M L: The relative importance of clinical, radiological and pulmonary function variables in evaluating asbestosis and chronic obstructive airway disease in asbestos workers. Clin Sci 41: 509-582, 1971. 485

REID D D, ANDERSON D O, FERRIS B G and FLETCHER C M: An Anglo-American comparison of the prevalence of bronchitis. Br Med J 2: 1487-1491, 1964. 486

REID D D, CORNFIELD J, MARKUSH R E, SEIGEL D, PEDERSEN E and HAENSZEL W: Studies of disease among migrants and native population in Great Britain, Norway, and the United States. III. Prevalence of cardiorespiratory symptoms among migrants and native-born in the United States. In National Cancer Institute Monograph No. 19: 321-346, 1966. 487

RIMINGTON J: Chronic bronchitis, smoking and social class. A study among working people in the towns of Mid and East Cheshire. Br J Dis Chest 63: 193-205, 1969. 488

RYDER R, LYONS J P, CAMPBELL H and GOUGH J: Emphysema in coal workers' pneumoconiosis. Br Med J 3: 481-87, 1970. 489

WALKER D D, ARCHIBALD R M and ATTFIELD M D: Bronchitis in men employed in the coke industry. Br J Ind Med 28: 358-63, 1971. 490

V-D. MORBIDITY STATISTICS IN OTHER FOREIGN COUNTRIES

The prevalence of respiratory symptoms has been investigated in several countries. As in the United States and Great Britain, there are several causes of respiratory symptoms including cigarette smoking, air pollution and industrial hazards.

1. Canada. As in the United States, there is an increasing mortality from bronchitis and emphysema in Canada (Gauthier, 1970; Neri et al., 1970). The morbidity statistics are less extensive in Canada. Anderson and others (1965) surveyed 246 males and 311 females in Chilliwack, British Columbia. Chronic respiratory disease was found to affect 29.3% of men and 18% of women between 25 and 79 years of age. The authors concluded that cigarette smoking was the most important single factor associated with respiratory diseases. Smoking caused a higher prevalence of respiratory symptoms in the following groups: 200 men and women 70 to 89 years old (Aguzzi et al., 1966); 310 male physicians 25 to 74 years old (Lefcoe and Wonnacott, 1970); 1,015 male employees in asbestos mines and mills (McDonald et al., 1972); and 1,138 Eskimos (Beaudry, 1968). The respective roles of air pollution, respiratory infections and social status have not been elucidated in these reports.

2. Sweden. The twin registry in Sweden has provided an unusual opportunity to investigate the morbidity among monozygotic and dizygotic pairs. In a group of 71 monozygotic twins with discordant smoking habits, there were more complaints of coughing and bronchitis

from the twins who smoke or who smoke most (Cederlof et al., 1965; Lundman, 1966). In a survey of 9,168 individuals entered in the registry, the prevalence of the respiratory symptoms was higher among male smokers in urban than in rural areas. A specific urban factor was interacting in some way with smoking (Cederlof, 1966). The hypermorbidity among smokers was found also among smokers in smoking-discordant monozygotic twin pairs (Cederlof et al., 1966, 1967). The American twin registry revealed a similar conclusion (Cederlof et al., 1969; International Symposium, 1971).

The following surveys indicate a higher incidence of respiratory illness in smokers than in nonsmokers: 339 men 50 years old (Wilhelmsen and Tibblin, 1966; Wilhelmsen et al., 1969), 240 iron mine workers (Jörgensen and Svensson, 1970), and 22,250 urban and rural residents (Irnell and Kiviloog, 1968). In the last two reports, the extent of air pollution influenced the morbidity from cigarette smoking.

3. Finland. In a rural population and among area pulp mill workers, there is a difference in prevalence of respiratory symptoms both in smokers and in nonsmokers. The higher incidence in the industrial area may relate either to the pollution in the air or to the fact that it is in the Arctic area (Huhti, 1965, 1966; Huhti et al., 1970). In these surveys as well as in those conducted by Järvinen et al. (1966) and Ruikka et al. (1966), smoking was found to increase the incidence of respiratory illness.

4. France. The higher prevalence of chronic bronchitis among smokers as compared with nonsmokers has been reported by Fréour et al. (1966), Kourilsky et al. (1966), Coudray et al. (1969), Brille (1969, 1970), Brille et al., 1970, Fournier and Zivy (1970), Golli (1970), Jancik (1970), and Vigy (1970). All of these reports confirm the observations previously made in the United States and Great Britain.

5. Germany. More than 30,000 questionnaires from 10 clinics of different towns in West Germany were analyzed (Ulmer and Reif, 1966). The nature of occupation influences the incidence of obstructive emphysema. Specific occupational types have been surveyed by others: asbestos workers (Hany et al., 1967), coal miners (Ulmer et al., 1968; Ulmer and Reichel, 1970; Ulmer, 1970) and chemical factory workers (Possner, 1970). The role of industrial exposure and cigarette smoking in the pathogenesis of pulmonary emphysema in Germany has been discussed by Wendel (1966).

6. Other Western European countries. In the Netherlands, Biersteker (1968, 1969) and Biersteker et al. (1969) reported an association between smoking and symptoms of chronic bronchitis among 1,000 male municipal employees. In Denmark, a group of 802 males and females over 50 years of age showed a lower ventilatory function in smokers than in nonsmokers (Hagerup and Larsen, 1971). In Copenhagen, a group of 156 welders was compared with a group of 152 other workers from the same plant (Fogh et al., 1969). The

PREGOWSKI W, BRYSIEWICZ, CESARZ-TRONCZYK M, KORDECKA J, LESZCBINSKI B, LUKJAN Z and SADOKIERSKA H: La bronchite chronique parmi les ouvriers d'une usine textile. Dépistage clinique et radiologique. Rev Tuberc Pneum 34: 753-5, 1970. 569

PRINSLOO I and LAUBSCHER N F: Emphysema in South African gold miners. In: Pneumoconiosis, edited by H A Shapiro, Cape Town, Oxford University Press, London, 380-5, 1970. 570

PUDELSKI J, OKLEK K and DELOFF L: Obraz epidemiologiczny przewlekłych nieswoistych chorób płuc u mieszkańców miasta zabrza. (Epidemiological situation of chronic non-specific diseases of the lung in inhabitants of the town of Zabrze.) Gruzlica 39: 604-9, 1971. 571

RODRÍGUEZ R L, ACHÓN P M, RODRÍGUEZ S H, DE LA PAZ E, PITA DE LA VEGA H, DURAND O R and SOLLET G R: Hábito de fumar y diagnóstico precoz del cáncer pulmonar alta. Estudio de 453 casos. Rev Cuba Med 8: 559-67, 1969. 572

RUIKKA I, SOURANDER L B and KASANEN A: The health of the aged in Turku. Ann Acad Sci Fenn Series A, 120: 1-50, 1966. 573

SLUIS-CREMER G K and SICHEL H S: Ventilatory function in males in a Witwatersrand town. Am Rev Resp Dis 98: 229-39, 1968. 574

SLUIS-CREMER G K, WALTERS L G and SICHEL H S: Chronic bronchitis in miners and non-miners: an epidemiological survey of a community in the gold-mining area in the Transvaal. Brit J Indust Med 24: 1-12, 1967a. 575

SLUIS-CREMER G K, WALTERS L G and SICHEL H S: Ventilatory function in relation to mining experience and smoking in a random sample of miners and non-miners in a Witwatersrand town. Brit J Industr Med 24: 13-25, 1967b. 576

STANEK V, FODOR J, HEJL Z, WIDIMSKY J, CHARVAT P, SANTRUCEK M, ZAJIC F and VAVRIK M: A contribution to the epidemiology of chronic bronchitis. Acta Med Scand 179: 737-46, 1966. 577

STANESCU D C, PILAT L, GAVRILESCU N, TECULESCU D B and CRISTESCU I: Aspects of pulmonary mechanics in arc welders' siderosis. Brit J Industr Med 24: 143-7, 1967. 578

STROBEL M and GSELL O: Mortalität in Beziehung zum Tabakrauchen 9 Jahre Beobachtungen bei Ärzten in der Schweiz. Helv Med Acta 32: 547-92, 1965. 579

SZYMCZYKIEWICZ K E, KUNSKI H and GIELEC L: Clinical evaluation of the respiratory system in cotton workers. Pol Med Sci Hist 13: 110-4, 1970. 580

TAKENOUCHI S: Epidemiological studies on chronic respiratory disturbances among employees in a certain organization's workshop. J Nara Med Assoc 19: 749-63, 1968. 581

TSUMETOSHI Y, SHIMIZU T, TAKAHASHI H, ICHINOSAWA A, UEDA M, NAKAYAMA H, YAMAGATA Y and OHSHINO A: Epidemiological study of chronic bronchitis with special reference to effect of air pollution. International Arch Arbeitsmedizin 29: 1-27, 1971. 582

ULMER W T: Emphysema of the lung: clinical and experimental investigations of its pathogenesis. Geriatrics 25: 164-9, 1970. 583

ULMER W T and REICHEL G: Zur Epidemiologie der chronischen bronchitis und deren Zusammenhang mit der Luftverschmutzung. (The epidemiology of chronic bronchitis and its relationship to air pollution.) Deutsche Med Wschr 95: 2549-54, 1970. 584

ULMER W T, REICHEL G and WERNER U: Die chronisch obstruktive bronchitis des Bergmannes. Untersuchungen zur Häufigkeit bei der Normalbevölkerung und bei Bergleuten. Die Bedeutung der Staubbelastung und der Einflub des Rauchens. (Chronic obstructive bronchitis of the coal miner.. An epidemiologic study of its incidence in the normal population and in coal miners. The importance of dust and smoking. Int Arch Gewerbepath Gewerbehyg 25: 75-98, 1968. 585

ULMER W T and REIF E: Epidemiologische Untersuchungen zur klinischen Bedeutung des chronisch obstruktiven Lungenemphysems. (Epidemiologic study of the clinical importance of chronic obstructive emphysema.) Beitr Klin Tuberk 133: 180-202, 1966. 586

VALIC F and ZUSKIN E: Byssinosis: a follow-up study of workers exposed to fine grade cotton dust. Thorax 27: 459-63, 1972. 587

VIGY M: Tabac, bronchite chronique et emphysème. Concours Med 3: 31-7, 1970. 588

VYSKOCIL J: Vztah pracovnich podminek k onemocneni bronchitidou a emfyzemem plic. (Relationship between working-conditions, bronchitic-disease and lung-emphysema.) Prac Lek 20: 41-7, 1968. 589

WALSHE M M and HAYES J A: Respiratory symptoms and smoking habits in Jamaica. Am Rev Resp Dis 96: 640-4, 1967. 590

WENDEL H: Beziehungen zwischen Nikotinabusus und Lungenemphysem. Z Gesamte Inn Med 21: 777-80, 1966. 591

WILHELMSEN L, ORHA I and TIBBLIN G: Decrease in ventilatory capacity between ages of 50 and 54 in representative sample of Swedish men. Brit Med J 3: 553-6, 1969. 592

WILHELMSEN L and TIBBLIN G: Tobacco smoking in fifty-year-old men. I. Respiratory symptoms and ventilatory function tests. Scand J Resp Dis 47: 121-30, 1966. 593

WOOLCOCK A J, BLACKBURN C R, FREEMAN M H, ZYLSTRA W and SPRING S R: Studies of chronic (nontuberculous) lung disease in New Guinea populations. Am Rev Resp Dis 102: 575-90, 1970. 594

ZWI S, SLUIS-CREMER G K and DU PREEZ L: A survey of pulmonary function in male office workers. Med Proceedings 13: 569-74, 1967. 595

VI: BRONCHOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

There are several investigations comparing measurements of bronchopulmonary function in smokers and nonsmokers. The results are discussed in this section, as distinct from those contrasting patients having pulmonary emphysema or chronic bronchitis with healthy controls (see Sections II and III). The separation is not a common practice because of the widespread belief that in smokers there is an abnormal bronchopulmonary condition representing the early stages of chronic bronchitis or pulmonary emphysema. There is no clinical or experimental support for this assumption.

With regard to the literature on this topic, it is important to point out that in the follow-up of smokers who show subnormal bronchopulmonary functioning there is no report of a subject who has developed chronic bronchitis and pulmonary emphysema. Most of the available articles deal with a comparison of smokers and nonsmokers executed once without a follow-up. The bibliographic list containing articles which serve as a background to this section is as follows:

No. 13. Pulmonary functional test.

VI-A. VENTILATORY FUNCTION

Several reports have appeared describing the effects of cigarette smoking on lung function. The conclusions are varied and depend on the manner of comparing smokers with nonsmokers. This discussion considers the importance of age, sex, height, environment and country of origin in determining the influence of cigarette smoking on pulmonary ventilation.

1. Age, sex, height and environment. A group of 302 subjects in Australia was investigated by Read and Selby (1961). The results were expressed as regression coefficients for mean expiratory flow based on age and height. Smokers without symptoms did not differ significantly from nonsmokers. However, smokers who complained of coughing with or without expectoration had lower ventilatory function than nonsmokers. The authors concluded that smoking alone does not reduce ventilatory function and suggested that a combination of genetic and environmental factors would produce symptoms and signs of decreased ventilatory function.

Cotes et al. (1966) have calculated the ventilatory capacities standardized to the average age, height and weight. They found the regression coefficient calculated separately for nonsmokers, light-to-moderate smokers and heavy smokers to be practically the same. This manner of testing the significance of the difference between smokers and nonsmokers has been overlooked by others who have correlated ventilatory capacities with age only.

Boren et al. (1966) reported the measurements of 266 subjects in the United States, specifying their age, height and smoking habits. They noted that vital capacity, inspiratory capacity and forced expiratory rate were slightly smaller and the functional residual capacity and residual volume were slightly lower in smokers than they were in nonsmokers. The differences were explained by the difference in mean age of nonsmoking subjects, which was lower than that of any of those who smoked.

In Finland, 420 men and 608 women, ranging in age from 40 to 64 years, were examined by Huhti (1967). On the basis of regression coefficients of age and height, there was no difference in forced vital capacity, one-second forced expiratory volume and peak expiratory flow between smokers and nonsmokers. A group of 44 young male recruits in Roumania was investigated by Stanescu et al. (1968). Lung volumes and ventilatory capacities of smokers did not differ from those of nonsmokers.

2. Age and environment. Flick and Paton (1959) reported the first comparison of ventilatory tests in a group of 222 male patients at a Veterans Hospital in the United States. The maximal expiratory flow was statistically different only between 60 and 70 years of age: the mean value for 20 nonsmokers was 378 l/min and that for 61 smokers was 258 l/min. Subjects from 20 to 50 years did not show a significant difference in their maximal expiratory flow.

Smoking in the older age group (40 to 60 years) has been shown by other investigators to reduce ventilatory function: Franklin

and Lowell (1961) in 376 male employees in Massachusetts; Catlett and Kidera (1969) in 257 male flight officers. Larson (1963) noted a difference in ventilatory function between smokers and nonsmokers, starting with the 30-year-old group in California. However, the difference cannot be attributed to smoking alone. The role of air pollution is difficult to assess in these reports, but one additional report has defined its influence. Anderson and Ferris (1965) compared the results of pulmonary function tests in a group in New Hampshire and another group in Canada. After controlling variations in age, sex and smoking habits, there were still significant differences in values of forced expiratory volume and peak expiratory flow rate. These differences could be explained by ethnic factors and atmospheric pollution.

3. Absence of age grouping. A survey of 262 American physicians, ranging in age from 25 to 79 years, showed that smokers have lower ventilatory function than nonsmokers (McIlreath and Cohen, 1966). In another group of 410 volunteers in an American community, ranging in age from 20 to 103 years, there was a decrease in ventilatory function of smokers (Edelman et al., 1966). A similar conclusion was arrived at in the examination of the following: 350 males in Pennsylvania 50 years or over (Weiss et al., 1963), 20 medical students or doctors in Massachusetts 18 to 45 years (Zwi et al., 1964), 140 males and females in Connecticut 67 to 95 years (Kiss, 1966), 150 males in India 15 to 50 years of age (Mohanty and Gupta, 1968), 298 females in Canada 25 to 59 years of age (Woolf and Suero, 1971), and 365 students in Connecticut

occurrence of respiratory symptoms in the welders and in the controls was associated with the cigarette smoking.

In Norway, Haenszel and Hougen (1972) concluded that the prevalence of respiratory symptoms was related to urban residence and to the amount of cigarettes consumed. In Spain, Bouhuys et al. (1969 a, b) noted that in a group of 216 hemp workers the associated disabling respiratory disease is attributable not to smoking habits but to prolonged exposure to hemp dust. In Switzerland, prospective studies of 3,479 doctors (Strobel and Gisell, 1965) and 1,885 residents of Basle (Mannhart, 1962) revealed a higher incidence of chronic lung disease among smokers than among nonsmokers.

7. Eastern Europe. In Poland, most surveys were conducted among workers with the following industrial connections: port and shipyard (Dobrzyński et al., 1970a), grain elevator (Dobrzyński et al., 1970b), wool industry (Brysiewicz et al., 1970), textile (Cierniak et al., 1970;, Szymczykiewicz et al., 1970), plaster works (Owsinski et al., 1971) and steel works (Council of Scientific Research, 1972). The workers who smoked cigarettes showed a higher rate of incidence of respiratory symptoms than nonsmokers. There are surveys which include residents of Bialystok (Pregowski et al., 1970), Warsaw (Kucewicz, 1969 a, b), Lublin (Durda and Szafranski, 1971), and Zarze (Pudelski et al., 1971).

In Czechoslovakia, epidemiological studies have been conducted as follows: 473 men 60 to 64 years old in Prague (Stanek et al., 1966); 441 men 50 to 65 years old in Prague (Boudik et al., 1970); 112 miners in Karvina (Pochmon et al., 1968); 3,466 hospital patients in Katowicach (Gasinska and Gburek, 1970); 2,376 persons in Brno (Vyskocil, 1968; Jancik and Jancik-Mak, 1972); and 95 men residing in Klin (Feuereisl et al., 1972). In the last-mentioned study, 5 men out of 51 who smoked 292,000 to 584,000 cigarettes during their lifetime showed no objective signs of chronic bronchitis.

The surveys in the U.S.S.R. (Petrova, 1956; Danovich et al., 1969; Futoransky et al., 1971), Roumania (Jelea et al., 1964; Stanescu et al., 1967), and Yugoslavia (Kalačić, 1970; Valic and Zuskin, 1972) have revealed an association between smoking and symptoms of chronic lung disease.

8. Middle East and Africa. Workers in South African gold mines have been examined by several investigators. Chatgidakis (1960) noted at autopsy that smokers with silicosis had lungs characterized by enlarged bronchial mucus glands. The enlargement was also seen in nonsmokers. In a survey of 827 males, chronic bronchitis was more common in miners than in nonminers in the same smoking category (Zwi et al., 1967; Sluis-Cremer et al., 1967 a, b; Sluis-Cremer and Sichel, 1968). The severity of emphysema in gold miners detected at autopsy was not related to smoking habits (Prinsloo and Laubscher, 1970).

In Egypt, a group of 223 cement workers showed a significant correlation between cement exposure and wheezing, dyspnea and physical signs of chronic bronchitis. Cigarette smoking was related only to cough and expectoration (El-Sewefy and Awad, 1971). Among 89 bricklayers and 245 workers in the rolling mills, respiratory symptoms were more frequently encountered among smokers than among nonsmokers (El-Sewefy, 1970). In Israel, among 257 cotton mill workers and 64 orchestra players, smoking was a significant factor which increased the prevalence of respiratory symptoms (Chwat and Mordish, 1971). Results of a survey of 175 Indian wool workers are similar (Mathur and Misra, 1972).

9. Asian-Pacific countries. In Australia, the following types of industrial workers have been examined: coalminers (Outhred and Flynn, 1960; McKenzie et al., 1969); felt manufacturers (Gandevia and Milne, 1965), and cotton workers (Barnes and Simpson, 1968). Residents in New South Wales (Hong et al., 1967; Gandeva, 1969) and in Sydney (Lake, 1969) have also been surveyed. An association between cigarette smoking and prevalence of chronic lung disease is indicated.

The results of surveys conducted in Japan (Takenouchi, 1968; Nishimoto et al., 1970; Tsumetoshi et al., 1971), in Singapore (Da Costa, 1972), in New Zealand (De Hamel et al., 1972) and in New Guinea (Woolcock et al., 1970) have revealed a relationship between smoking and prevalence of respiratory symptoms.

10. South America and Caribbean. The epidemiological studies, reported from Mexico (Paras Chavero et al., 1970/ Celis et al./ 1971; 1968), Cuba (Rodriguez Rivera et al., 1969), Chile (Oyanguren et al., 1972) and Jamaica (Walshe and Hayes, 1967) reveal an association between smoking and prevalence of respiratory symptoms.

BIBLIOGRAPHY

V. NON-OCCURRENCE OF CHRONIC PULMONARY DISEASE IN SMOKERS

D. MORBIDITY STATISTICS IN OTHER FOREIGN COUNTRIES

Reprint

AGUZZI G, WOOLF C R and PATERSON J F: The prevalence and type of chronic obstructive bronchopulmonary disease in very old people. Canad Med Ass J 94: 932-9, 1966. 491

ANDERSON D O, FERRIS JR B C and ZICKMANTEL R: The Chilliwack respiratory survey, 1963: Part IV. The effect of tobacco smoking on the prevalence of respiratory disease. Canad Med Ass J 92: 1066-76, 1965. 492

BARNES R and SIMPSON G R: Ventilatory capacity changes on exposure to cotton dust. Med J Australia 1: 897-900, 1968. 493

BEAUDRY P H: Pulmonary function survey of the Canadian Eastern Arctic Eskimo. Arch Environ Health 17: 524-8, 1968. 494

BIERSTEKER K: Bronchitisklachten bij Rotterdams gemeentepersoneel. (Symptoms of bronchitis among municipal personnel in Rotterdam.) Ned T Geneesk 112: 1208-11, 1968. 495

BIERSTEKER K: Air pollution and smoking as cause of bronchitis. Arch Environ Health 18: 531-5, 1969. 496

BIERSTEKER K, VAN GEUNS H A and VAN LEEUWEN P: Cough and peak flow rates of municipal employees in Rotterdam. Environ Res 2: 272-6, 1969. 497

BOUDIK F, GOLDSMITH J R, TEICHMAN V and KAUFMANN P-C: Epidemiology of chronic bronchitis in Prague. Bull WHO 42: 711-22, 1970. 498

BOUHUYS A, BARBERO A, SCHILLING R S and VAN DE WOESTIJNE K P: Chronic respiratory disease in hemp workers. Am J Med 46: 526-37, 1969a. 499

BOUHUYS A, SCHILLING R S and VAN DE WOESTIJNE K P: Cigarette smoking, occupational dust exposure, and ventilatory capacity. Arch Environ Health 19: 793-7, 1969. 500

BRILLE D: Fréquence de la bronchite chronique chez la femme rôle du tabac. Rev Tuberc et Pneumol 33: 794-6, 1969. 501

BRILLE D: Possibilites du depistage au stade initial de la bronchite chronique et de l'emphysème pulmonaire. (Possibilities of detection in the early stages of chronic bronchitis and pulmonary emphysema.) Rev Med 11: 2201-10, 1970. 502

BRILLE D, COUDRAY P, ISRAEL-ASSELAIN R, LE MELLETIER J, MICHEL F B, MIGUÈRES J, PHAM G T and VOISIN C: Colloques sur la bronchite chronique. I. -- Nosologie et épidémiologie. Rev Tuberc Pneumol 34: 723-48, 1970. 503

BRYSIEWICZ K, BULUK H, CESARZ-FRONCZYK M, KORDECKA J, LESZCZYŃSKI B, ŁUKJAN Z and SADOKIERSKA H: Wpływ Pracy W Warunkach Zapylenia Na Częstość Występowania Przewlekłych Zapaleń Oskrzeli U Pracowników Zakładów Przemysłu Wełnianego Im. Sierżana W Białymstoku. (The effect of occupation in dustiness on the prevalence of chronic bronchitis among the workmen of the Sierżan's establishments of wool industry at Białystok.) Gruzlica 38: 657-61, 1970. 504

CEDERLÖF R: Urban factor and prevalence of respiratory symptoms and "angina pectoris." Arch Environ Health 13: 743-8, 1966. 505

CEDERLÖF R, EDFORS M-L, FRIBERG L and JONSSON E: Hereditary factors, "spontaneous cough" and "smoker's cough". Arch Environ Health 14: 401-6, 1967. 506

CEDERLÖF R, FRIBERG L and HRUBEC Z: Cardiovascular and respiratory symptoms in relation to tobacco smoking. A study on American twins. Arch Environ Health 18: 934-40, 1969. 507

CEDERLOF R, FRIBERG L, JONSSON E and KAIJ L: Morbidity among monozygotic twins. Arch Environ Health 10: 346-50, 1965. 508

CEDERLOF R, FRIBERG L, JONSSON E and KAIJ L: Respiratory symptoms and "angina pectori" in twins with reference to smoking habits. An epidemiological study with mailed questionnaire. Arch Environ Health 13: 726-37, 1966. 509

CELIS S A, DÍAZ O J, GOROCICA D and CANO V F: Enfisema pulmonar y contaminacion aerea. Neumol Cir Torax 29: 135-41, 1968. 510

CHATGIDAKIS C B: A study of the bronchial mucous glands in white South African gold miners. Arch Environ Health 1: 335-42, 1960. 511

CHWAT M and MORDISH R: Respiratory symptoms and byssinosis among textile workers in Israel. Harefuah 80: 559-62, 586-7, 1971. 512

CIERNIAK E, JELONKIEWICZ J, SŁODCZYK M, CIERNIAK J and PAWLAK F: Przewlekłe Zapalenie Oskrzeli Wśród Pracowników Zakładów Włókienniczych. (Chronic bronchitis in the workmen of textile industry.) Gruzlica 38: 635-41, 1970. 513

COUDRAY P, SERISE M and FRÉOUR P: Recherche épidémiologique sur les bronchites chroniques et les insuffisances respiratoires. Étude de prévalence dans un échantillon de femmes de 30 a 70 ans. Rev Tuberc Pneumol 33: 769-80, 1969. 514

COUNCIL O F SCIENTIFIC RESEARCH ON CHRONIC NONSPECIFIC RESPIRATORY DISEASES IN CRACOW, POLAND: Przewlekle Nieswoiste Choroby Ukladu Oddechowego Wsrod Mieszakancow Krakowa. XVI. Wyniki Badania Przekrojowego w Hucie im Lenina. (Chronic nonspecific respiratory diseases in the inhabitants of Cracow, XVI. Results of a cross section study in the Lenin steel works.) Przeglad Epidemiologiczny 26: 125-34, 1972. 515

DA COSTA J L: Chronic obstructive lung disease (COLD): A comparison between men and women. Singapore Med J 13: 74-8, 1972. 516

DANOVICH B Z, KOROVINA O V, SMIRNOV I P and ANISIMOVA N A: On the epidemiology of chronic nonspecific diseases of the lungs. Teraper Arkhiv 41: 63-8, 1969. 517

DEHAMEL F A and O'DONNELL T V: Smoking habits and respiratory symptoms of Dunedin public servants. New Zealand Med J. 76: 1-4, 1972. 518

DOBRZYŃSKI W, KISIELEWICZ J and KOCIECKA I: Analiza Kliniczno-Statystyczna Przewlekłych Niezytow Oskrzeli U Pracowników Portu I Stoczni W Szczecinie. (Clinical and statistical analysis of chronic bronchitis in port and shipyard workers.) Medycyna Pracy 21: 294-306, 1970a. 519

Reprint

DOBRZYŃSKI W, KISIELEWICZ J and KOCIECKA I: Przewlekłe Zapalenia Oskrzeli U Pracowników Portowego Elewatora Zbożowego. (Chronic bronchitis among the workmen of a harbour grain elevator.) Gruzlica 38: 651-6, 1970b. 520

DURDA M and SZAFRAŃSKI W: Przewlekłe nieswoiste choroby płuc wśród ludności wiejskiej woj. lubelskiego. (Chronic non-specific diseases of the lung among the rural population of the Lublin Voivodship.) Gruzlica 39: 616-20, 1971. 521

EL-SEWEFY A Z: Chest symptomatology in a Sheffield steel works (S. P. T.). J Egyp Med Assoc 52: 578-81, 1970. 522

EL-SEWEFY A Z and AWAD S: Chest symptomatology in an Egyptian Portland cement factory. J Egyp Med Assoc 54: 457-64, 1971. 523

FEUEREISL R, KRZHIVANEK I, REIL I, KUBIK A and FELKEL K: Effect of smoking on the cardiopulmonary function. Klinicheskaya Meditzina 50: 82-4, 1972. 524

FOGH A, FROST J and GEORG J: Respiratory symptoms and pulmonary function in welders. Ann Occup Hyg 12: 213-8, 1969. 525

FOURNIER E and ZIVY P: Poumon et tabac. (Lung and tobacco). Poumon Coeur 26: 1109-25, 1970. 526

FRÉOUR P, COUDRAY P, ROUSSEL A and SERISÉ A: Les bronchites chroniques et l'insuffisance respiratoire dans l'agglomération de Bordeaux. J Med Bordeaux 143: 1865-79, 1966. 527

FUTORYANSKY Y I, DETSIK Y I, SHUFLAT A N, SIMONCHIK V N and BARANSKY S M: Effect of smoking on the ventilation function of the lungs. Klinicheskaya Meditsina 49: 70-4, 1971. 528

GANDEVIA B: A productive cough upon request as an index of chronic bronchitis: the effects of age, sex, smoking habit and environment upon prevalence in Australian general practice. Med J Australia 1: 16-20, 1969. 529

GANDEVIA B and MILNE J: Ventilatory capacity on exposure to jute dust and the relevance of productive cough and smoking to the response. Brit J Industr Med 22: 187-95, 1965. 530

GAUTHIER H: L'insuffisance respiratoire au Canada. Laval Med 41: 992-4, 1970. 531

GASIŃSKA T and GBUREK Z: O Szkodliwości Przewlekłego Palenia Tytoniu. (On the harmful effects of chronic tobacco smoking.) Wiad Lek 23: 2157-62, 1970. 532

GOLLI V: Étude épidémiologique des bronchopathies non spécifiques. Bronches 20: 313-30, 1970. 533

HAENSZEL W and HOUGEN A: Prevalence of respiratory symptoms in Norway. J Chronic Dis 25: 519-44, 1972. 534

HAGERUP L and LARSEN M: Tobaksrygning og respiratoriske symptomer i en dansk population. (Tobacco smoking and respiratory symptoms in a Danish population.) Ugeskr Laeg 133: 1302-6, 1971. 535

HANY A, BURCKHARDT P and BUHLMANN A: Zur Klinik und Pathophysiologie der Lungenasbestose. Schweiz Med Wochenschr 97: 597-603, 1967. 536

HONG C S, GANDEVIA B and LOVELL H: Ventilatory capacity in a series of male adults and the effect of respiratory symptoms, productive cough, smoking habit and occupation. Med J Australia 1: 169-72, 1967. 537

HUHTI E: Prevalence of respiratory symptoms, chronic bronchitis and pulmonary emphysema in a Finnish rural population. Field survey of age group 40-64 in the Harjavalta area. Acta Tuberc Pneumol Scand Suppl 61: 101 pp., 1965. 538

HUHTI E: Chronic respiratory disease among old people in a Finnish rural area. Ann Med Int Fenn 55: 99-105, 1966. 539

HUHTI E, RYHANEN P, VUOPALA U and TAKKUNEN J: Chronic respiratory disease among pulp mill workers in an arctic area in Northern Finland. Acta Med Scand 187: 433-44, 1970. 540

INTERNATIONAL SYMPOSIUM IN SAN JUAN: Twin registries in the study of chronic disease. With particular reference to the relation of smoking to cardiovascular and pulmonary diseases. Acta Med Scand Suppl. 523: 40 pp., 1971. 541

IRNELL L and KIVILOOG J: Bronchial asthma and chronic bronchitis in a Swedish urban and rural population. With special reference to prevalence, respiratory function and socio-medical condition. Scand J Resp Dis (Suppl) 66: 86pp., 1968. 542

JANCIK E: Quelques données et corrélations provenant d'une étude épidémiologique sur l'incidence des symptômes caractéristiques des maladies respiratoires chroniques non spécifiques. Rev Tuberc Pneum 34: 749-52, 1970. 543

JANCIK E and JANCIK-MAK M: Chronische unspezifische lungenerkrankungen. (Chronic non-specific lung diseases). Praxis Pneumologie 26: 69-81, 1972. 544

JARVINEN K A, PATIALA J and THOMANDER K: The role of chronic smoking in the etiology of obstructive pulmonary emphysema. A study of 3,375 persons. Ann Med Intern Fenn 49: 307-311, 1966. 545

JELEA A, ILIE E and GAVRILĂ F: Contribuţii la studiul insuficienţei pulmonare de etiologie tabagică. (Contributions to the study of pulmonary insufficiency of tabacic etiology.) Medicina Internă 16: 229-34, 1964. 546

JÖRGENSEN H and SVENSSON A: Studies on pulmonary function and respiratory tract symptoms of workers in an iron ore mine where diesel trucks are used underground. J Occup Med 12: 348-54, 1970. 547

KALAČIĆ I: Kronični bronhitis i ventilacijska funkcija pluća u pušača i nepušača. (Chronic bronchitis and ventilatory lung function in smokers and nonsmokers.) Arh Hig Rada 21: 5-12, 1970. 548

KOURILSKY R, BRILLE D and HATTE M J: Etude statistique de la relation entre le tabac et la bronchite chronique. Bull Acad Nat Med 150: 318-29, 1966. 549

KUCEWICZ J: Przewlekłe Nieswoiste Choroby Układu Oddechowego Wśród Mieszkańców Krakowa. VIII. Metoda Dyskryminacyjna Fishera W Analizie Wpływu Palenia Tytoniu na Występowanie Objawów Chorobowych. (Chronic nonspecific respiratory diseases in the city of Cracow.) Przeg Epid 23: 331-7, 1969a. 550

KUCEWICZ J: Chronic nonspecific respiratory diseases in the city of Cracow. Epidemiol Rev 23: 159-65, 1969b. 551

LAKE B: Morbid conditions at death in old men. J Chronic Dis 21: 761-79, 1969. 552

LEFCOE N M and WONNACOTT T H: The prevalence of chronic respiratory disease in the male physicians of London, Ontario. Canad Med Assoc J 102: 381-5, 1970. 553

LUNDMAN T: Smoking in relation to coronary heart disease and lung function in twins. Acta Med Scand 180 (Suppl. 455): 1-75, 1966. 554

MANNHART M: Krankheiten in ihrer Beziehung zu Genubmitteln in der Bevölkerung von Basel. Enquête bei erwachsenen Personen 1956 und 1961. Zeitschrift fur klinische Medizin 157: 240-57, 1962. 555

MATHUR K C and MISRA S N: Incidence of pulmonary diseases among wool workers. Indian J Chest Dis 14: 172-8, 1972. 556

MCDONALD J C, BECKLAKE M R, FOURNIER-MASSEY G and ROSSITER C E: Respiratory symptoms in chrysotile asbestos mine and mill workers of Quebec. Arch Environ Health 24: 358-63, 1972. 557

MCKENZIE H I, GLICK M and OUTHRED K G: Chronic bronchitis in coal miners: ante-mortem/post-mortem comparisons. Thorax 24: 527-35, 1969. 558

NERI L C, MANDEL J S, O'CONNOR M L and LARSON M: A household survey of chronic obstructive pulmonary disease in Ottawa: Methodological problems and results of pilot survey. Canad J Pub Health 61: 407-12, 1970. 559

NISHIMOTO Y, BURROWS B, MIYANISHI M, KATSUTA S, SHIGENOBU T and KETTEL L J: Chronic obstructive lung disease in Japanese poison gas workers. Am Rev Resp Dis 102: 173-9, 1970. 560

OUTHRED K G and FLYNN M J: Some aspects of chronic respiratory diseases in coalminers in New South Wales, Australia. Dis Chest 37: 390-9, 1960. 561

OWSIŃSKI J, JANUŚ T and MYSIK M: Występowanie przewlekłych nieswoistych chorób ukladu oddechowego (p. n. ch. u. o.) wśród pracowników Zakladu Przemyslu Gipsowego ,, Dolina Nidy" w Gackach. (Occurrence of chronic unspecific diseases of the respiratory system among workers in the plaster works at Dolina Nidy in Gacki.) Przeg Lek 28: 476-80, 1971. 562

OYANGUREN H, DONOSO H, PRIETO L, VARGAS S and PAZ S: Prevalencia de la bronquitis cronica en un area urbana y una rural de Santiago y su relacion con el grado de contaminacion atmosferica. (Prevalence of chronic bronchitis in urban and rural areas of Santiago: Its relation with the degree of air pollution). Rev Med Chile 100: 101-5, 1972. 563

PARÁS C E, MERCADO C E and QUINTERO N A: Tabaquismo y Cardiopatia Coronaria. Arch Inst Cardiol Mex 40: 128-34, 1970. 564

PARÁS C E, MERCADO E and QUINTERO A: Simposio sobre problemas medicos originados por el tabaquismo. II. Alteraciones cardiovasculares. Neumol Cir Tórax Méx 32: 15-8, 1971. 565

PETROVA A: Influence of occupational hazards in tobacco fermentation factories in Bulgaria (town Plovdiv) on the organism of the workers. 69-81, 1956. 566

POCHMON V, SKARABELLOVA M and LEGOSTOV J: Chronic obstructive bronchitis in miners of Karvine District. Prac Lekar 20: 366-71, 1968. 567

POSSNER W: Betrachtungen und Ergebnisse zur Epidemiologie nichtspezifischer Erkrankungen der Atemwege. Z Ges Hyg 16: 545-52, 1970. 568

15 to 18 years of age (Seely et al., 1971). However, the age and height of smokers and nonsmokers were not matched, so that it is not possible to specify the age when smoking influences ventilatory function.

The technique of pairing a smoker with a nonsmoker of the same age and sex has been used by two groups of investigators. Wilson et al. (1960) reported 14 pairs in Texas all over 40 years old and noted a decrease in timed expiratory volume, total lung capacity and maximal breathing capacity. Carey et al. (1967) reported 7 pairs in Ireland ranging from 19 to 60 years of age. Ventilatory capacity measured daily was less in smokers than in nonsmokers. The size of the group does not permit the conclusion as to the age when smoking starts to influence ventilatory capacity.

4. Abstinence from smoking. In some smokers with abnormal ventilatory function, cessation of smoking caused an improvement (Peters and Miller, 1960; Wynder et al., 1967; Peterson et al., 1968; Schuman, 1971). Administration of bronchodilator drugs has also reduced the airway obstruction in smokers (Petty et al., 1970). The abnormalities in ventilatory function associated with smoking are reversible.

BIBLIOGRAPHY

VI. BRONCHOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

A. VENTILATORY FUNCTION

Reprint

ANDERSON D O, and FERRIS B G Jr: Air pollution levels and chronic respiratory disease. Arch Environ Health 10: 307-11, 1965. 596

BOREN H G, KORY R C and SYNER J C: The Veterans administration-army cooperative study of pulmonary function. II: The lung-volume and its subdivisions in normal men. Am J Med 41: 96-114, 1966. 597

CAREY G C R, DAWSON T A J and MERRETT J D: Daily changes in ventilatory capacity in smokers and in non-smokers. Br J Prev Soc Med 21: 86-89, 1967. 598

CATLETT G F and KIDERA G J: Detection of respiratory impairment in pilots. Aerosp Med 40: 1252-57, 1969. 599

COTES J E, ROSSITER C E, HIGGINS I T T and GILSON J C: Average normal values for the forced expiratory volume in white Caucasian males. Br Med J 1: 1016-19, 1966. 600

EDELMAN N H, MITTMAN C, NORRIS A H, COHEN B H and SHOCK N W: The effects of cigarette smoking upon spirometric performance of community dwelling men. Am Rev Resp Dis 94: 421-29, 1966. 601

FLICK A L and PATON R R: Obstructive emphysema in cigarette smokers. Arch Intern Med 104: 518-26, 1959. 602

FRANKLIN W and LOWELL F C: Unrecognized airway obstruction associatied with smoking: a probable forerunner of obstructive pulmonary emphysema. Ann Intern Med 54: 379-86, 1961. 603

HUHTI E: Ventilatory function in healthy nonsmokers and smokers. Scand J Resp Dis 48: 149-55, 1967. 604

KISS G T: Pulmonary survey in the aged. Dis Chest 49: 305-8, 1966. 605

LARSON R K: The chronic effect of cigarette smoking on pulmonary ventilation. Am Rev Resp Dis 88: 630-35, 1963. 606

McILREATH F J and COHEN B M: Ventilatory performance of American physicians. Am J Med Sci 252: 1-8, 1966. 607

MOHANTY P and GUPTA T C: Smoking habit and pulmonary ventilation in Adivasis. Indian J Physiol Pharmacol 12: 87-89, 1968. 608

PETERS G A and MILLER R D: Effect of smoking on asthma and emphysema. Proc Mayo Clin 35: 353-58, 1960. 609

PETERSON D I, LONGERGAN L H and HARDINGE M G: Smoking and pulmonary function. Arch Environ Health 16: 215-18, 1968. 610

PETTY T L, BRINK G A, MILLER M W and CORSELLO P R: Objective functional improvement in chronic airway obstruction. Chest 57: 216-23, 1970. 611

Bibliography VI-A

Reprint

READ J and SELBY T: Tobacco smoking and ventilatory function of the lungs. Br Med J 2: 1104-8, 1961. 612

SCHUMANN L M: The benefits of cessation of smoking. Chest 59: 421-27, 1971. 613

SEELY J E, ZUSKIN E and BOUHUYS A: Cigarette smoking: Objective evidence for lung damage in teen-agers. Science 172: 741-43, 1971. 614

STANESCU D C, GAVRILESCU N and TECULESCU D N: Effect of smoking on pulmonary mechanics and ventilation in young healthy males. Respiration 25: 434-40, 1968. 615

WEISS W, BOUCOT K R, COOPER D A, and CARNAHAN W J: Smoking and the health of older men. II. Smoking and ventilatory function. Arch Environ Health 7: 538-47, 1963. 616

WILSON R H, MEADOR R S, JAY B E and HIGGINS E: The pulmonary pathologic physiology of persons who smoke cigarettes. N Engl Med J 262: 956-61, 1960. 617

WOOLF C R and SUERO J T: The respiratory effects of regular cigarette smoking in women. Am Rev Resp Dis 103: ; 26-37, 1971. 618

WYNDER E L, KAUFMAN P L and LESSER R L: A short-term follow-up study on ex-cigarette smokers. With special emphasis on persistent cough and weight gain. Am Rev Resp Dis 96: 645-55, 1967. 619

ZWI S, GOLDMAN H I and LEVIN A: Cigarette smoking and pulmonary function in healthy young adults. Am Rev Resp Dis 89: 73-81, 1964. 620

VI-B. AIRWAY RESISTANCE

That cigarette smoking reduces forced expiratory volume in certain individuals described in the preceding section indicates a bronchospastic component. The other techniques used to investigate airway resistance are discussed in this section.

1. Body plethysmograph technique. The measurement of airway resistance or airway conductance by body plethysmograph technique is more sensitive than others applicable to man. All reports uniformly show an increase in resistance or a decrease in conductance in smokers as compared with nonsmokers: Pelzer and Thomson (1966) reporting from England on 82 subjects 17 to 82 years of age; Sevčik (1967) from Czechoslovakia on 150 men 18 to 68 years of age; Guyatt and Alpers (1968) and Guyatt et al. (1970) from England on 752 men 38 to 67 years old; Allen and Sabin (1971) from Texas on 32 males and females 16 to 82 years old; Diamond et al. (1971) from Kentucky on 30 subjects 19 to 44 years old; Huttemann et al. (1971, 1972) from Germany on 20 subjects 20 to 40 years old. The extent of increase in resistance varies with the age of the individual and the country of origin. The bronchoconstriction is readily reversed by abstinence from smoking for a few days (Cohen, 1966; Wilhelmsen, 1967; McFadden and Linden, 1972) or by the inhalation of a bronchodilator drug (Curtis et al., 1966; Crompton, 1968; Woolcock et al., 1969; Ruff et al., 1972).

2. Acute effects of cigarette smoking in man detected by various techniques. Immediately after inhalation of cigarette smoke, there is an increase in airway resistance in normal subjects, both smokers and nonsmokers (Attinger et al., 1958; Sterling, 1967; Chiang and Wang, 1970; Reintjes et al., 1972; Da Silva and Hamosh, 1973). The bronchoconstriction was reduced by prior administration of atropine, indicating that the vagus nerve participates in the response (Sterling, 1967). Filtration of the smoke to remove either the particulate or the vapor phase had a similar effect in reducing the bronchoconstrictor response, showing that both phases contribute to this response (Clarke et al., 1970). Inhalation of isoproterenol prevented the response, which reflects its reversibility (Nadel and Comroe, 1961).

The acute bronchoconstriction has been reported following inhalation of cigarette smoke in patients with chronic lung disease: Simonsson (1962, 1965) reporting from Sweden; Cellereno and Billia (1962) from Italy; McDermott and Collins (1965) from Great Britain; Johannsen (1966) from Poland; James (1970) from Ohio; and Votchal et al. (1970) from the Soviet Union. These effects are transient in nature and do not necessarily contribute to the abnormal ventilatory function.

3. Acute and chronic effects of inhalation of cigarette smoke in animals. The author of this review and his collaborators reported the effects of inhalation of cigarette smoke in several animal species:

dog (Aviado and Palecek, 1967; Klide and Aviado, 1968; Cho et al., 1968; Carrillo and Aviado, 1970); cat (Palecek and Aviado, 1967); rabbit (Palecek et al., 1967); and rat (Aviado and Carrillo, 1969; Shore and Aviado, 1969; Aviado et al., 1970). The bronchoconstriction is brought about by the following mechanisms: (a) stimulation of cholinergic receptors in the airways; (b) stimulation of sensory receptors in the lungs, which triggers reflex spasm and (c) release of histamine, which produces bronchospasm (Aviado and Samanek, 1965; Samanek and Aviado, 1965; Samanek et al., 1965). Simultaneously, bronchodilatation is also produced by stimulation of adrenergic mechanisms arising from nicotine contained in the cigarette smoke and by reflex mechanism.

Following chronic exposure to cigarette smoke, there is an increase in airway resistance in rats (Ito and Aviado, 1968; Aviado, 1972) and mice (Aviado, 1972). This effect is reversed by inhalation of sympathomimetic drugs. The results in animals serve to explain the reversibility of bronchoconstriction as seen in man and described in the above paragraphs.

VI. BRONCHOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

B. AIRWAY RESISTANCE

Reprint

ALLEN G W and SABIN S: Comparison of direct and indirect measurement of airway resistance. Am Rev Resp Dis 104: 61-71, 1971. 621

ATTINGER E O, GOLDSTEIN M M, and SEGAL M S: Effects of smoking upon the mechanics of breathing. I. In normal subjects. Am Rev Tuberc Pulm Dis 77: 1-16, 1958. 622

AVIADO D M: Bronchovascular effects of cigarette smoke. CTR Grant No. 599 Progress Report No. 4, June 1, 1971 -April 15, 1972, 19 pages 623

AVIADO D M and CARRILLO L R: Hormones and pulmonary effects of tobacco. Arch Environ Health 18: 925-33, 1969. 624

AVIADO D M and PALECEK F: Pulmonary effects of tobacco and related substances. Arch Environ Health 15: 187-93, 1967. 625

AVIADO D.M, SADAVONGVIVAD C and CARRILLO L R: Cigarette smoke and pulmonary emphysema. Influence of bronchodilators and biogenic amines in experimental induction in rats. Arch Environ Health 20: 483-87, 1970. 626

AVIADO D M and SAMANEK M: Bronchopulmonary effects of tobacco and related substances. Arch Environ Health 11: 141-51, 1965. 627

AVIADO D M, WATANABE T and BELEJ M A: Bronchovascular effects of cigarette smoke. CTR Grant # 599 Prog. Rep. # 5, 27 pages, 1973. 628

CELLERINO A and BILLIA P: Volumi polmonari in fumatori sani e broncopatici prima e dopo uso di filtro chimico per sigarette. Minerva Med 53: 1516-21, 1962. 629

CHIANG S T and WANG B C: Acute effects of cigarette smoking on pulmonary function. Am Rev Resp Dis 101: 860-67, 1970. 630

CHO Y W, SAMANEK M and AVIADO D M: Differences in the effects of inhalation of sulfur dioxide and cigarette smoke. Arch Environ Health 16: 651-55, 1968. 631

CLARKE B G, GUYATT A R, ALPERS J H, FLETCHER C M and HILL I D: Changes in airways conductance on smoking a cigarette. A study of repeatability and of the effect of particulate and vapour phase filters. Thorax 25: 418-22, 1970. 632

COHEN B M and ROCHESTER M D: Sympathomimetic amine aerosol administration in chronic obstructive ventilatory disease. Med Times 94: 355-59, 1966. 633

CROMPTON G K: A comparison of responses to bronchodilator drugs in chronic bronchitis and chronic asthma. Thorax 23: 46-55, 1968. 634

CURTIS J K, ASHLEY P L, RASMUSSEN H K and CREE E M: The bronchospastic component in patients with chronic bronchitis and emphysema. JAMA 197: 693-97, 1966. 635

DA SILVA A M T and HAMOSH P: Effect of smoking a single cigarette on the 'small airways'. J Appl Physiol 34: 361-65, 1973. 636

DIAMOND L, LIPSCOMB W and JOHNSON R: Acute pulmonary effects of smoking a reference cigarette. Toxicol Appl Pharmacol 18: 638-48, 1971. 637

GUYATT A R and ALPERS J H: Factors affecting airways conductance: a study of 752 working men. J Appl Physiol 24: 310-16, 1968. 638

GUYATT A R, BERRY G, ALPERS J H, BRAMLEY A C and FLETCHER C M: Relationship of airway conductance and its immediate change on smoking habits and symptoms of chronic bronchitis. Am Rev Resp Dis 101: 44-54, 1970. 639

HUTTEMANN U, OSWALD P, LODE H and HUCKAUF H: Veranderungen der lungenfunktion jugendlicher als folge langjahrigen zigarettenrauchens. (Changes in pulmonary function of young people as a result of cigarette smoking over many years). Deutsche Med Wochenschrift 96: 1791-93, 1971. 640

HUTTEMANN U, OSWALD P, LODE H and HUCKAUF H: Uber den einfluss langjahrigen zigarettenrauchens auf die lungenfunktion jugendlicher normalpersonen. (Lung function studies in young apparently healthy cigarette smokers versus nonsmokers). Respiration 29: 270-87, 1972. 641

ITO H and AVIADO M: Pulmonary emphysema and cigarette smoke. Experimental induction and use of bronchodilators in rats. Arch Environ Health 16: 865-70, 1968. 642

JAMES R H: Prior smoking as a determinant of the distribution of pulmonary ventilation. Am Rev Resp Dis 101: 105-7, 1970. 643

JOHANNSEN Z and PREIBISZ J: Bezposredni wplyw palenia papierosow na spirogram u zdrowych i chorych z rozedma pluc i przewleklym niezytem oskrzeli. (A direct effect of smoking on spirometric values in normal subjects and patients with pulmonary emphysema and chronic bronchitis). Pol Arch Med Wzwn 36: 783-86, 1966. 644

KLIDE A M and AVIADO D M: Carotid receptors and bronchomotor responses. Effects of cigarette smoke, lobeline, and cyanide. Arch Environ Health 17: 65-70, 1968. 645

McDERMOTT M and COLLINS M M: Acute effects of smoking on lung airways resistance in normal and bronchitic subjects. Thorax 20: 562-69, 1965. 646

McFADDEN E R Jr and LINDEN D A: A reduction in maximum mid-expiratory flow rate. A spirographic manifestation of small airway disease. Am J Med 52: 725-37, 1972. 647

MILLER J M and SPROULE B J: Acute effects of inhalation of cigarette smoke on mechanical properties of the lungs. Am Rev Resp Dis 94: 721-26, 1966. 648

NADEL J A and COMROE J H Jr: Acute effects of inhalation of cigarette smoke on airway conductance. J Appl Physiol 16: 713-16, 1961. 649

PALECEK F and AVIADO D M: Pulmonary effects of tobacco and related substances. II. Comparative effects of cigarette smoke, nicotine, and histamine on the anesthetized cat. Arch Environ Health 15: 194-203, 1967. 650

PALECEK F, OSKOUI M and AVIADO D M: Pulmonary effects of tobacco and related substances. III. Inhibition of synthesis of histamine in various species. Arch Environ Health 15: 204-13, 1967. 651

PELZER A M and THOMSON M L: Effect of age, sex, stature, and smoking habits on human conductance. J Appl Physiol 21: 469-76, 1966. 652

REINTJES M, SEIERENGA J and BOGAARD J M: Effect of smoking one cigarette on airway resistance. Scand J Resp Dis 53: 129-34, 1972. 653

ROBERTSON D G, WARRELL D A, NEWTON-HOWES J S and FLETCHER C M: Bronchial reactivity to cigarette and cigar smoke. Br Med J 3: 269-71, 1969. 654

RUFF F, SALEM A, BUSY F, de VERNEJOUL P, EVEN P and BROUET G: La fermeture des voies aeriennes peripheriques son augmentation chez les fumeurs. (Airway closure and its increase in smokers). Rev Tuberc Pneumol 36: 308-11, 1972. 655

SAMANEK M and AVIADO D M: Bronchopulmonary effects of tobacco and related substances. II. Bronchial arterial injection of nicotine and histamine. Arch Environ Health 11: 152-59, 1965. 656

SAMANEK M, AVIADO D M and PESKIN G W: Bronchopulmonary effects of tobacco and related substances. Arch Environ Health 11: 160-76, 1965. 657

SEVCIK M: Vliv koureni na funkci plic a bronchospasmus zjistovany pomoci farmkodynamickeho testu. (Influence of smoking on pulmonary function and bronchospasm ascertained by a pharmacodynamic test). Scripta Med Fac Med Brunensis 40: 265-77, 1967. 658

SHORE S R and AVIADO D M: Hormones and pulmonary effects of tobacco. II. Progesterone. Arch Environ Health 19: 59-69, 1969. 659

SIMONSSON B: Effect of cigarette smoking on the forced expiratory flow rate. Am Rev Resp Dis 85: 534-39, 1962. 660

SIMONSSON B G: Clinical and physiological studies on chronic bronchitis. III. Bronchial reactivity to inhaled acetylcholine. Acta Allergol 20: 325-48, 1965. 661

STERLING G M: Mechanism of bronchoconstriction caused by cigarette smoking. Br Med J 3: 275-77, 1967. 662

VOTCHAL B E, LOZINSKY L G, GRIBOVA O A, TAGAI V A and SHEFER Y M: Condition of bronchial patency in young people. Terap Arkhiv 42: 39-43, 1970. 663

WILHELMSEN L: Effects on bronchopulmonary symptoms, ventilation and lung mechanics of abstinence from tobacco smoking. Scand J Resp Dis 48: 407-14, 1967. 664

WOOLCOCK A J, VINCENT N J and MACKLEM P T: Frequency dependence of compliance as a test for obstruction in the small airways. J Clin Invest 48: 1097-1105, 1969. 665

VI-C. BRONCHIAL CLEARANCE

Cigarette smoking retards the clearance mechanism in certain experimental conditions. The effects of cigarette smoking on ciliary motility and mucus secretion are part of the defense mechanisms in the lung against inhalants in general and air pollutants in particular. (Gross, 1967; Gross and Hatch, 1963; Kilburn, 1967, 1968).

1. Mucociliary transport in man. The first observations relating to the effect of cigarette smoking on the respiratory epithelium were made in vitro (Rakieten et al., 1912). Strips of the nasal mucosa were examined under the microscope. The solution through which cigarette smoke was passed did not influence ciliary activity for a 5- to 10-min period. Longer exposure caused cessation of ciliary activity. These results were difficult to relate to the usual manner of smoking. Ballenger (1960) introduced another in vitro technique, using fresh mucosa scraped under general anesthesia from the trachea of children. The ciliotoxicity from the smoked solution is also difficult to relate to the usual form of smoking.

The introduction of radioactive particles for measurement of bronchial clearance has made it possible to investigate the influence of cigarette smoking in man. The results so far have not been consistent. Albert et al. (1969a) used monodisperse ferric oxide aerosols (0.8 to 7.9 μ): bronchial clearance was impaired in 8 out of 14 cigarette smokers. Pavia et al. (1970, 1971) and Thomson and Pavia (1973) used radioactive polystyrene particles 5 μ in diameter. There was no demonstrable difference in mucociliary transport between smokers

and nonsmokers. Lourence et al. (1971) used particles 2 μ in size and noted that the clearance was delayed in smokers as compared with nonsmokers. Camner and Philipson (1971) and Camner et al. (1971, 1973) used 6 to 7 μ particles and observed a faster clearance immediately following smoking. However, habitual smokers showed an increase in clearance three weeks after abstaining. There appear to be two kinds of effects produced by cigarette smoking, an acute type which accelerates and a chronic type which decelerates clearance. Mucociliary transport in the nasal cavity is either retarded by smoking (Evert, 1965) or not influenced by it (Quinlan et al., 1969).

In 10 monozygotic pairs of twins that were discordant with regard to cigarette smoking, half of the smoking pairs had a markedly slower clearance than the nonsmokers, whereas the other half had a similar clearance (Camner and Philipson, 1972; Camner et al., 1972). It has not been possible to obtain a consistent effect from cigarette smoking even by comparing a smoker with a nonsmoker who is constitutionally similar.

2. Mucociliary transport in the rabbit. The results in animals are also variable. There was no effect from two hours' exposure to cigarette smoke on ciliary activity in vivo in the rabbit (Dalhamn, 1964) and on bronchial clearance of radioactive particles in the same species (LaBelle et al., 1966). A depression has been reported by others, using different techniques for measuring ciliary activity (Krueger and Smith, 1958) and clearance (Holma, 1969).

The functional activity of the ciliated epithelium can be influenced by oxygen tension (Dalhamn and Rosengren, 1968), particulate matter (Falke et al., 1959), and acetylcholine (Kordek et al., 1952). Cigarette smoke can exert its influence through any one or more of these mechanisms and this may account for the varied results reported in the rabbit. Kensler and Battista (1963), by using smoke filters, concluded that the ciliotoxic activity is in the gaseous phase. The following constituents of smoke depress ciliary activity in the rabbit: carboxylic acid and aldehydes (Wynder et al., 1965), phenol (Dalhamn, 1966) and acrolein (Scharbort, 1967).

3. Mucociliary transport in the cat. The observations in the cat have consistently shown a depression of bronchial clearance by exposure to cigarette smoke (Dalhamn, 1964, 1966; Carson et al., 1966; Kaminski et al., 1968). The tar content of the cigarette smoke influenced its ciliotoxicity (Nakashima, 1938; Dalhamn and Rylander, 1964, 1965, 1967, 1968). This effect was not simulated by nicotine but could be prevented by oxolamine citrate (Dalhamn, 1968, 1969). The role of the volatile constituents in cigarette smoke has been debated (Kensler and Battista, 1966; Dalhamn and Rylander, 1967, 1970; Kensler, 1967). Some chemical constituents of cigarette smoke have been shown to interact in their effect on mucociliary transport, which might explain the varied action reported for cigarette smoke (Weissbecker et al., 1971).

4. Mucociliary transport in other animal species. The following animal species have been used in investigation of the influence of cigarette smoke: rat (Dalhamn and Rhodin, 1956; Dalhamn, 1959; Ferin et al., 1966; Guillerm et al., 1961); guinea pig (Hilding and Filipi, 1966); cow (Hill, 1928; Mendenhall and Shreeve, 1937; Hilding, 1956 a, b); monkey (Kensler and Battista, 1966); chicken (Battista and Kensler, 1970 a, b); donkey (Albert et al., 1969 b, 1973; Frances et al., 1970); and invertebrates (Boche and Quilligan, 1959; Wynder et al., 1963, 1965; Walker and Kiefer, 1966; Dalhamn, 1967; Weiss, 1968; Krahl and Bulmash, 1969; Kennedy and Elliott, 1970). Ciliary activity consistently shows a depression by cigarette smoke but bronchial clearance is influenced in a variable manner, the latter by ciliary activity and mucus formation, as discussed in Section III.

BIBLIOGRAPHY

VI. BRONCHOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

C. BRONCHIAL CLEARANCE

Reprint

ALBERT R E, ALESSANDRO D, LIPPMANN M and BERGER J: Long-term smoking in the donkey. Arch Environ Health 22: 12-19, 1971. 666

ALBERT R E, LIPPMANN M and BRISCOE W: The characteristics of bronchial clearance in humans and the effects of cigarette smoking. Arch Environ Health 18: 738-55, 1969. 667

ALBERT R E, LIPPMANN M, PETERSON H T Jr, BERGER J, SANBORN K and BOHNING D: Bronchial deposition and clearance of aerosols. Arch Int Med 131: 115-27, 1973. 668

ALBERT R E, SPIEGELMAN J R, SHATSKY S and LIPPMANN M: The effect of acute exposure to cigarette smoke on bronchial clearance in the miniature donkey. Arch Environ Health 18: 30-41, 1969. 669

BALLENGER J J: Experimental effect of cigarette smoke on human respiratory cilia. N Engl J Med 263: 832-35, 1960. 670

BATTISTA S P and KENSLER C J: Use of the nonimmersed in vitro chicken tracheal preparation for the study of ciliary transport activity. Arch Environ Health 20: 318-25, 1970. A. 671

BATTISTA S P and KENSLER C J: Mucus production and ciliary transport activity. In vivo studies using the chicken. Arch Environ Health 20: 326-33, 1970 B. 672

BOCHE R D and QUILLIGEN J J Jr: The effects of air pollutants on tissue cultures. Fed Proc Bull 18: 559, 1959. 673

CAMNER P and PHILIPSON K: Humanstudier av tracheobronchiell clearance med monodispersa terflonpartiklar markta med 18_F och 99_{mTc}. (Tracheobronchial clearance in man studied with monodispersed teflon particles tagged with 18_F and 99_{mTc}. Nord Hyg Tidskr 52: 1-9, 1971. 674

CAMNER P and PHILIPSON K: Tracheobronchial clearance in smoking-discordant twins. Arch Environ Health 25: 60-63, 1972. 675

CAMNER P, PHILIPSON K and ARVIDSSON T: Cigarette smoking in man. Short-term effect on mucociliary transport. Arch Environ Health 23: 421-26, 1971. 676

CAMNER P, PHILIPSON K and ARVIDSSON T: Withdrawal of cigarette smoking. A study of tracheobronchial clearance. Arch Environ Health 26: 90-92, 1973. 677

CAMNER P, PHILIPSON K and FRIBERG L: Tracheobronchial clearance in twins. Arch Environ Health 24: 82-87, 1972. 678

CARSON S, GOLDHAMER R and CARPENTER R: Mucus transport in the respiratory tract. Am Rev Resp Dis 93: 86-92, 1966. 679

CRESS H R, SPOCK A and HEATHERINGTON D C: The localization of succinic dehydrogenase, cytochrome oxidase and adenosine triphosphatase in ciliated respiratory epithelium. J Histochem Cytochem 13: 677-83, 1965. 680

DALHAMN T: The effect of cigarette smoke on ciliary activity in the upper respiratory tract. Arch Otolaryngol 70: 166-68, 1959. 681

DALHAMN T: Studies on tracheal ciliary activity. Am Rev Resp Dis 89: 870-77, 1964. 682

DALHAMN T: Effect of cigarette smoke on ciliary activity. Am Rev Resp Dis 93: 108-14, 1966. 683

DALHAMN T: Effect of different doses of tobacco smoke on ciliary activity in cat. Variations in amount of tobacco smoke, interval between cigarettes, content of "tar", nicotine, and phenol. Natl Cancer Inst Monogr 28: 79-87, 1968. 684

DALHAMN T: The anticillostatic effect of cigarettes treated with oxolamine citrate. Am Rev Resp Dis 99: 447-48, 1969. 685

DALHAMN T: Ciliostatic effect of phenol and resorcinol. Arch Otolaryngol 84: 325-32, 1966. 686

DALHAMN T and RHODIN J: Mucous flow and ciliary activity in the trachea of rats exposed to pulmonary irritant gas. Br J Ind Med 13: 110-13, 1956. 687

DALHAMN T and ROSENGREN A: The effect of oxygen lack on the tracheal ciliary activity. Arch Environ Health 16: 371-73, 1968. 688

DALHAMN T and RYLANDER R: Ciliastatic action of smoke from filter-tipped and non-tipped cigarettes. Nature 201: 401-2, 1964. 689

DALHAMN T and RYLANDER R: Ciliastatic action of cigarette smoke. Arch Otolaryngol 81: 379-82, 1965. 690

DALHAMN T and RYLANDER R: Tar content and ciliotoxicity of cigarette smoke. Acta Pharmacol Toxicol 25: 369-72, 1967. 691

DALHAMN T and RYLANDER R: Reply. Arch Environ Health 14: 372-73, 1967. 692

DALHAMN T and RYLANDER R: Ciliotoxicity of cigarette smoke and its volatile components. Am Rev Resp Dis 98: 509-11, 1968. 693

DALHAMN T and RYLANDER R: Ciliotoxicity of cigar and cigarette smoke. Arch Environ Health 20: 252-53, 1970. 694

DALHAMN T, RYLANDER R and SPEARS A W: Differences in ciliotoxicity of cigarette smoke. Am Rev Resp Dis 96: 1078-79, 1967. 695

EVERT G: On the mucous flow rate in the human nose. Acta Otolaryngol 300: 1- 1965. 696

FALK H L, TREMER H M and KOTIN P: Effect of cigarette smoke and its constituents on ciliated mucus-secreting epithelium. J Natl Cancer Inst 23: 999-1012, 1959. 697

FERIN J: The mechanism of elimination of deposited particles from the lungs. Ann Occup Hyg 10: 207-16, 1967. 698

FERIN J, URBANKOVA G, VICKOVA A and REICHRTOVA E: The effect of cold and cigarette smoke on the elimination of dust from the lungs. Pracov Lek 18: 263-64, 1966. 699

FRANCES R, ALESSANDRO D, LIPPMANN M, PROCTOR D E and ALBERT R E: Effect of cigarette smoke on particle transport on nasociliary mucosa of donkeys. Arch Environ Health 21: 25-31, 1970. 700

GROSS P: Le mecanisme du transport alveolaire. Poumon Coeur 23: 1215-27, 1967. 701

GROSS P and HATCH T: Pulmonary clearance: its mechanism and its relation to pulmonary disease. J Occup Med 5: 191-94, 1963. 702

GUILLERM R, BADRE R and VIGNON B: Effects inhibiteurs de la dumee de tabac sur l'activite ciliaire de l'epithelium respiratoire et nature des composants responsables. Bull Acad Natl Med 145: 416-23, 1961. 703

HILDING A C: On cigarette smoking, bronchial carcinoma and ciliary action: III. Accumulation of cigarette tar upon artificially produced deciliated islands in the respiratory epithelium. Ann Otololaryng 65: 116-30, 1956A. 704

HILDING A C: On cigarette smoking, bronchial carcinoma and ciliary action. II. Experimental study on the filtering action of cow's lungs the deposition of tar in the bronchial tree and removal by ciliary action. N Engl J Med 254: 1155-60, 1956B. 705

HILDING A C: The role of the respiratory mucosa. Minn Med 50: 915-19, 1967. 706

HILDING A C and FILIPI A N: A method of determining nasal filtration of cigarette smoke. Ann Otol 75: 714-24, 1966. 707

HILL L: The ciliary movement of the trachea studied in vitro. Lancet 2: 802-5, 1928. 708

HOLMA B: The acute effect of cigarette smoke on the initial course of lung clearance in rabbits. Arch Environ Health 18: 171-73, 1969. 709

KAMINSKI E J, FANCHER O E and CALANDRA J C: In vivo studies of the ciliastatic effects of tobacco smoke. Arch Environ Health 16: 188-93, 1968. 710

KENSLER C J: Cigarette smoke and ciliastasis. Arch Environ Health 14: 371- 73, 1967. 711

KENNEDY J R and ELLIOTT A M: Cigarette smoke: Residue on mitochondrial structure. Science 168: 1097-98, 1970. 712

KENSLER C J and BATTISTA S P: Components of cigarette smoke with ciliary-depressant activity. N Engl J Med 269: 1161-66, 1963. 713

KENSLER C J and BATTISTA S P: Chemical and physical factors affecting mammalian ciliary activity. Am Rev Resp Dis 93: 93-102, 1966. 714

KILBURN K H: Cilia and mucus transport as determinants of the response of lung to air pollutants. Arch Environ Health 14: 77-91, 1967. 715

KILBURN K H: A hypothesis for pulmonary clearance and its implications. Am Rev Resp Dis 98: 449-63, 1968. 716

KORDICK P, BULBRING E and BURN J H: Ciliary movement and acetycholine. Br J Pharmacol 7: 67-79, 1952. 717

KRAHL V E and BULMASH M H: Studies on living ciliated epithelium. Am Rev Resp Dis 99: 711-17, 1969. 718

KRUEGER A P and SMITH R F: Effects of gaseous ions on tracheal ciliary rate. Proc Soc Exp Biol Med 98: 412-14, 1958. 719

LaBELLE C W, BEVILACQUA D M and BRIEGER H: The influence of cigarette smoke on lung clearnace. Arch Environ Health 12: 588-96, 1966. 720

LOURENCE R V, KLIMER M F and BOROWSKI C J: Deposition and clearance of 2μ particles in the tracheobronchial tree of normal subjects -- smokers and nonsmokers. J Clin Invest 50: 1411-20, 1971. 721

MENDENHALL W L and SHREEVE K E: The effect of cigarette smoke on the tracheal cilia. J Pharmacol Exp Ther 60: 111-12, 1937. 722

MOOLTEN S E: Pulmonary lymphatics in relation to pulmonary clearance interstitial fluid and the pathogenesis of emphysema. Pub Health Serv 1787: 191-221, 1968. 723

NAKASHIMA T: Pharmacological studies on the ciliary movement. Jap J Med Sci Sect Pharmacol 11: 42, 1938. 724

PAVIA D, SHORT M D and THOMSON M L: No demonstrable long term effects of cigarette smoking on the mucociliary mechanism of the human lung. Nature 226: 1228-31, 1970. 725

PAVIA D, THOMSON M L and POCOCK S J: Evidence for temporary slowing of mucociliary clearance in the lung caused by tobacco smoking. Nature 231: 325-26, 1971. 726

QUINLAN M F, SALMAN S D, SWIFT D L, WAGNER H N Jr, and PROCTOR D F: Measurement of mucociliary function in man. Am Rev Resp Dis 99: 13-23, 1969. 727

RAKIETEN N, RAKIETEN M L, FELDMAN D and BOYKIN M J Jr: Mammalian ciliated respiratory epithelium. Arch Otolaryngol 56: 494-503, 1912. 728

SCHARBORT J C: Lactic dehydrogenase from human lung inhibition by certain water-soluble ciliastatic components of tobacco smoke. J South Africa Chem Inst 20: 103-112, 1967. 729

THOMSON M L and PAVIA D: Long-term tobacco smoking and mucociliary clearance. From the human lung in health and respiratory impairment. Arch Environ Health 26: 86-89, 1973. 730

WALKER T R and KIEFER J E: Ciliastatic components in the gas phase of cigarette smoke. Science 153: 1248-50, 1966. 731

WEISS W: Cigarette smoke gas phase and paramecium survival. Arch Environ Health 17: 62-64, 1968. 732

WEISSBECKER L, CREAMER R M and CARPENTER R D: Cigarette smoke and tracheal mucus transport rate. Am Rev Resp Dis 104: 182-87, 1971. 733

WYNDER E L, GOODMAN D A and HOFFMANN D: Ciliatoxic components in cigarette smoke. II. Carboxylic acids and aldehydes. Cancer 18: 505-9, 1965. 734

WYNDER E L, GOODMAN D A and HOFFMANN D: Ciliatoxic components in cigarette smoke. III. In vitro comparison of different smoke components. Cancer 18: 1652-58, 1965. 735

WYNDER E L, KAISER H E, GOODMAN D A and HOFFMANN D: A method for determining ciliastatic components in cigarette smoke. Cancer 16: 1222-25, 1963. 736

VII. CARDIOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

This section is a continuation of Section VI on the differences between smokers and nonsmokers. Measurements of cardiopulmonary function include ventilation-perfusion relationship, pulmonary circulation, cardiac function, pulmonary function, surfactant and other constituents of the lung. It is important to point out that animal experiments have served to clarify the mode of action by which the constituents of cigarette smoke influence the heart and lungs. The following bibliographic lists contain articles on general aspects of the topic under consideration.

No. 14. Constituents of cigarette smoke.

No. 15. Cardiopulmonary effects of cigarette smoke.

VII-A. VENTILATION-PERFUSION RELATIONSHIPS

Measurement of pulmonary diffusion capacity shows a reduction in smokers compared with nonsmokers: Martt (1962) reporting from Missouri; Krumholz et al. (1964, 1965) from Indiana; Rankin et al. (1965) from Wisconsin; and Van Ganse et al. (1972) from the Netherlands. Anderson and Shephard (1969) reported from Canada that among 43 healthy adult men, by serial multiple regression analysis, pulmonary diffusion capacity correlated with age and weight. By using the predicted equation for diffusion coefficient, smoking habits had no substantial effect on diffusion capacity. Bates (1955) and McGrath and Thomson (1959) arrived at a similar conclusion with a limited number of subjects. It has also been suggested that the presence of carboxyhemoglobin in blood of smokers would account for the lower value for diffusion capacity.

Cigarette smokers show some inadequacy of gas mixing in the lung as compared with nonsmokers (Ross et al., 1967; Stănescu et al., 1968). There is also an alteration in the ventilation-perfusion ratio in smokers (Williams and Anderson, 1968 a, b; Anderson and Williams, 1969). The change has not been confirmed by others and the participation of pulmonary blood vessels in the phenomenon has not been proven.

Inhaling cigarette smoke by the use of a smoking device that brought more smoke into the lungs with each breath than would be the case in ordinary smoking did not significantly change blood gas exchange in normal subjects or patients with a moderate degree of emphysema (Motley and Kuzman, 1958). However, patients in California with severe emphysema showed decreases in arterial oxygen tension and saturation.

A similar hypoxemia was observed to arise from smoking by patients with chronic lung disease in Ireland (Chapman, 1965) by patients with chronic bronchitis in England (Penman and Howard, 1966), and by patients with chronic bronchitis in Massachusetts (Strieder and Kazemi, 1967; Strieder et al., 1968). Hypoxemia is characteristic of patients in whom it does not necessarily relate to smoking but to pathological lesions in the lung (Pain et al., 1967; Weiss and Dulfano, 1968; Poppius, 1969).

Postoperative complications are reported to be higher among nonsmokers than smokers in Great Britain (Morton, 1944; Piper, 1958; Wightman, 1968). Smokers from Sweden do not show a higher incidence of pulmonary postoperative complications (Wiklander and Norlin, 1957). It has been suggested that postoperative hypoxemia is related to the appearance of pulmonary complications among smokers in Australia (Morton, 1969).

VII. CARDIOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

A. VENTILATION-PERFUSION RELATIONSHIPS

Reprint

ANDERSON T W and SHEPHARD R J: Normal values for single-breath diffusing capacity - the influence of age, body size and smoking habits. Respiration 26: 1-7, 1969. 737

ANDERSON W H: Acute exposure to cigarette smoke as a cause of hypoxia. Chest 59: 33S-34S, 1971. 738

ANDERSON W H and WILLIAMS J B: Effects of cigarette smoke on distribution of pulmonary perfusion. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 75-9, 1969. 739

BATES D V, BOUCOT N G and DORMER A E: The pulmonary diffusing capacity in normal subjects. J Physiol 129: 237-52, 1955. 740

BURROWS B: Pulmonary diffusion and alveolar-capillary block. Med Clin N Am 51: 427-38, 1967. 741

CHAPMAN T T: The acute effect of cigarette smoking on pulmonary function. J Irish Med Assoc 56: 72-4, 1965. 742

DORMANDY T L: Abnormal oxygen-dissociation curves. Lancet 2: 80-1, 1965. 743

FORSTER R E, ROUGHTON F J, CANDER L, BRISCOE W A and KREUZER F: Apparent pulmonary diffusing capacity for CO at varying alveolar O_2 tensions. J Appl Physiol 11: 277-89, 1957. 744

HOLLAND J, MILIC-EMILI J, MACKLEM P T and BATES D V: Regional distribution of pulmonary ventilation and perfusion in elderly subjects. J Clin Invest 47: 81-92, 1968. 745

KRUMHOLZ R A, CHEVALIER R B and ROSS J C: Cardiopulmonary function in young smokers. A comparison of pulmonary function measurements and some cardiopulmonary responses to exercise between a group of young smokers and a comparable group of nonsmokers. Ann Internal Med 60: 603-10, 1964. 746

KRUMHOLZ R A, CHEVALIER R B and ROSS J C: Changes in cardiopulmonary functions related to abstinence from smoking. Studies in young cigarette smokers at rest and exercise at 3 and 6 weeks of abstinence. Ann Internal Med 62: 197-207, 1965. 747

MARTT J M: Pulmonary diffusing capacity in cigarette smokers. Ann Internal Med 56: 39-45, 1962. 748

McGRATH M W and THOMSON M L: The effect of age, body size and lung volume change on alveolar-capillary permeability and diffusing capacity in man. J Physiol 146: 572-82, 1959. 749

MORTON A: Postoperative hypoxaemia. Med J Australia 2: 341-2, 1969. 750

MORTON H J: Tobacco smoking and pulmonary complications after operation. Lancet 1: 368-70, 1944. 751

MOTLEY H L and KUZMAN W J: Cigarette smoke. Its effects on pulmonary function measurements. California Med 88: 211-20, 1958. 752

Bibliography VII-A

Reprint

PAIN M C, GLAZIER J B, SIMON H and WEST J B: Regional and overall inequality of ventilation and blood flow in patients with chronic airflow obstruction. Thorax 22: 453-61, 1967. 753

PENMAN R W: Regional and overall ventilation-perfusion ratios in normal subjects and patients with chronic lung disease. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U. S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 63-73, 1969. 754

PENMAN R W and HOWARD P: Distribution of pulmonary ventilation and blood flow in normal subjects and patients with chronic bronchitis. Clin Sci 30: 63-78, 1966. 755

PIPER D W: Respiratory complications in the post-operative period. Scottish Med J 3: 193-8, 1958. 756

POPPIUS H: Expiratory CO_2 curve in pulmonary diseases. Scand J Resp Dis 50: 135-46, 1969. 757

RANKIN J, GEE J B and CHOSY L W: The influence of age and smoking on pulmonary diffusing capacity in healthy subjects. Medicina Thoracalis 22: 366-74, 1965. 758

ROSS J C, LEY G D, KRUMHOLZ R A and RAHBARI H: A technique for evaluation of gas mixing in the lung: studies in cigarette smokers and nonsmokers. Am Rev Resp Dis 95: 447-53, 1967. 759

STANESCU D C, TECULESCU D B, PACURARU R and GAVRILESCU N: Chronic effect of smoking upon pulmonary distribution of ventilation in healthy males. Respiration 25: 497-504, 1968. 760

STRIEDER D J and KAZEMI H: Hypoxemia in young asymptomatic cigarette smokers. Ann Thoracic Surg 4: 523-31, 1967. 761

STRIEDER D J, MURPHY R and KAZEMI H: Hypoxemia in asymptomatic smokers. Clin Res 16: 376, 1968. 762

STUART-HARRIS C H: Pulmonary hypertension and chronic obstructive bronchitis. Am Rev Resp Dis 97: 9-17, 1968. 763

VAN GANSE W, DEPOORTER A M, MEHEUS A, EYLENBOSCH W, VANHOORNEEN M, VUYLSTEEK K, DE VREEZE G and RAVEEL E: Bijdrage van de pulmonaire diffusiecapaciteit (transferfactor van de long) in het kader van bevolkingsonderzoek naar CARA. (The role of the pulmonary diffusion capacity (transfer factor of the lung) in screening for CARA) Nederlands Tijdschrift voor Geneeskunde 116/28: 1167-72, 1972. 764

WEISS E B and DULFANO M J: Quantitative acid-base dynamics in chronic pulmonary disease. Ann Internal Med 69: 263-72, 1968. 765

WIGHTMAN J A: A prospective survey of the incidence of postoperative pulmonary complications. Brit J Surg 55: 85-91, 1968. 766

WIKLANDER O and NORLIN U: Effect of physiotherapy on post-operative pulmonary complications. A clinical and roentgenographic study of 200 cases. Acta Chirurgica Scand 112: 246-54, 1957. 767

WILLIAMS J B and ANDERSON W H: Acute effects of cigarette smoke on pulmonary ventilation-perfusion relationships. Am Rev Resp Dis 98: 145-6, 1968a. 768

WILLIAMS J B and ANDERSON W H: Acute effects of cigarette smoke on distribution of pulmonary perfusion. Clin Res 16: 377, 1968b. 769

VII-B. PULMONARY CIRCULATION

The pulmonary vascular lesions in pulmonary emphysema have been summarized by Liebow (1959). The lesions in the small pulmonary arteries are severe enough to cause elevation of pulmonary arterial blood pressure (Hicken et al., 1965). Electron microscopy has revealed damage to the endothelium, filling of the capillary lumina with collagen, and recanalization of the damaged vessels (Martin and Boatman, 1965). Crenshaw (1968) has reviewed the hypothesis that pulmonary emphysema has a vascular etiology. However, none of the vascular lesions seen in human pulmonary emphysema have been reproduced in animals by cigarette smoking. The lungs of healthy cigarette smokers show fibrous thickening which is also seen in the aging lungs of nonsmokers (Auerbach et al., 1968).

The acute effect of smoking one cigarette was studied in 67 Indian patients suffering from chronic bronchopulmonary disease (Viswanathan, 1965). There was a significant rise in mean and diastolic pressure in the pulmonary artery, but no significant change in systolic. The change in diastolic pressure was interpreted to mean vasoconstriction, although there was no measurement of cardiac output nor of left atrial pressure to allow estimation of pulmonary vascular resistance. The fall in pulmonary compliance seen among smokers does not relate to changes in the pulmonary circulation (Krumholz et al., 1965).

There are some observations relating to pulmonary circulation in animals exposed to cigarette smoking. Larson et al. (1965) used nicotine intravenously and noted a biphasic rise and then fall in pulmonary vascular resistance in the dog. Samanek and Aviado (1966) noticed a rise in pulmonary arterial blood pressure following inhalation of cigarette smoke, but the

response could not be repeated in the same animal for purposes of eliciting the mechanism of the rise. Nicotine injection was utilized and the following mechanisms were identified: vasoconstriction by release of catecholamine stores in the lung and the release of histamine.

BIBLIOGRAPHY

VII. CARDIOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

B. PULMONARY CIRCULATION

Reprint

AUERBACH O, HAMMOND E C and GARKINKEL L: Thickening of walls of arterioles and small arteries in relation to age and smoking habits. New Engl J Med 278: 980-4, 1968. 770

CRENSHAW G L: Vascular etiology of pulmonary emphysema. 1968. 771

HICKEN P, HEATH D, BREWER D B and WHITAKER W: The small pulmonary arteries in emphysema. J Path Bacteriol 90: 107-14, 1965. 772

KRUMHOLZ R A, CHEVALIER R B and ROSS J C: A comparison of pulmonary compliance in young smokers and nonsmokers. Am Rev Resp Dis 92: 102-7, 1965. 773

LARSON R K, FUKUDA P and MURRAY J F: Systemic and pulmonary vascular effects of nicotine in anesthetized dogs. Am Rev Resp Dis 91: 556-64, 1965. 774

LIEBOW A A: Pulmonary emphysema with special reference to vascular changes. Am Rev Resp Dis 80: 67-93, 1959. 775

MARTIN H B and BOATMAN E S: Electron microscopy of human pulmonary emphysema. Am Rev Resp Dis 91: 206-9, 1965. 776

SAMANEK M and AVIADO D M: Cardiopulmonary effects of tobacco and related substances. III. Pulmonary vascular effects of cigarette smoke and nicotine. Arch Environ Health 12: 717-24, 1966. 777

VISWANATHAN R: Acute effects of cigarette smoking on pulmonary artery pressures. Indian J Med Res 53: 421-7, 1965. 778

VII-C. CARDIAC FUNCTION

Since cigarette smoking has been identified as the most important cause of pulmonary emphysema by the United States Public Health Service, it has been implicated in cor pulmonale (Parade, 1969; Behnke et al., 1970). In a group of 150 patients with cor pulmonale in India, 28% were nonsmokers (Sanghvi and Kotia, 1963). In another group of 134 patients in India, 39% were nonsmokers (Khosla et al., 1969). In the United States the proportion of nonsmokers is lower among patients with cor pulmonale; Cullen et al. (1970) reported from New York only 3 out of 60 patients. Patients dying of cor pulmona have manifested failure of the left ventricle but the role of cigarette smoking has not been proven (Mitchell et al., 1968; Rao et al., 1969; Strong et al., 1969).

BIBLIOGRAPHY

VII. CARDIOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

C. CARDIAC FUNCTION

Reprint

CULLEN J H, KAEMMERLEN J T, DAOUD A and KATZ H L: A prospective clinical-pathologic study of the lungs and heart in chronic obstructive lung disease. Am Rev Resp Dis 102: 190-204, 1970. 779

INTER-SOCIETY COMMISSION FOR HEART DISEASE RESOURCES: Primary prevention of pulmonary heart disease. Circulation 41: A17-A23, 1970. 780

KHOSLA S N, MEHROTRA A N and ANKLESARIA X J: A clinical study of chronic cor pulmonale in Northern India. J Indian Med Assoc 53: 529-34, 1969. 781

MITCHELL R S, WALKER S H and MAISEL J C: The causes of death in chronic airway obstruction. II. Myocardial infarction. Am Rev Resp Dis 98: 611-2, 1968. 782

PARADE D: Cor pulmonale und Rauchen. Med Klin 64: 80-4, 1969. 783

RAO B S, COHN K E, ELDRIDGE F E and HANCOCK E W: Left ventricular failure secondary to chronic pulmonary disease. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U. S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 129-33, 1969. 784

SANGHVI L M and KOTIA K C: Heart failure in patients with chronic pulmonary emphysema. Dis Chest 44: 67-78, 1963. 785

STRONG J P, RICHARDS M L, MCGILL H C, EGGEN D A and MCMURRY M T: On the association of cigarette smoking with coronary and aortic atherosclerosis. J Atheroscler Res 10: 303-17, 1969. 786

VII- D. PULMONARY SURFACTANT AND OTHER CONSTITUENTS

Stability of the pulmonary alveoli is partially due to changes in surface tension. The surface active component of lung extract which is responsible for maintaining alveolar distension has been called surfactant. Bondurant (1960), Miller et al (1960) and Miller and Bondurant (1962) reported that the application of cigarette smoke to lung extract caused a decrease in surface tension. They also reported that lung extract prepared from rats which have been exposed to smoke in life have lower surface tension than that of unexposed rats. They concluded that these results may relate to the pathogenesis of pulmonary emphysema.

Subsequent reports have confirmed the reduction of surfactant in bronchial washings of the dog by in vitro application (Webb et al., 1967) and in the dog, cat and guinea pig by in vivo inhalation of cigarette smoke (Giammona, 1967; Sekulic et al., 1968). Two recent reports include the incorporation of radioactive labeled palmitic acid into pulmonary surfactant. Giammona et al. (1971) used unanesthetized dogs exposed repeatedly to cigarette smoke daily for 37 to 87 days. They noted no change in surface activity or in rate of time of incorporation of palmitic acid in these dogs. Balint et al. (1971) used anesthetized dogs and administered cigarette smoke by positive ventilation from 90 to 220 min. They reported a decrease in choline and phosphate incorporation in the lecithin of the lung. The results in the unanthestetized dog are similar to the effects obtained by the usual use of tobacco in man, whereas those in the anesthetized dog are toxicological in nature.

Measurement of surfactant activity in man has been made on bronchial washings. Cook and Webb (1966) noted a decrease of surfactant action in nonsmokers with lung disease and in chronic smokers with or without demonstrable pulmonary disease. A reduction in the white layer of the lavage fluid after centrifugation has been reported in smokers (Pratt et al., 1969). There is a deficit in total lipid content, particularly of lecithin, in the lavage from smokers as compared with that from nonsmokers (Finley and Ladman, 1972). These observations have been commented upon by Clements (1972), Sachs (1972) and Finley (1972) in relation to the shortcomings of using lavage fluid in interpreting the events occurring in the alveolar lining.

There are other reported changes in the lung of patients with chronic lung disease. The reduction in tissue content of cadmium and zinc in patients with chronic bronchitis or pulmonary emphysema by Szadkowski et al. (1969). Lewis et al. (1969), and Morgan (1971) have not been examined in the lungs of smokers without lung disease. Inhalation of cigarette smoke causes a release of histamine from lung tissue (Aviado et al., 1966) and from the guinea pig lung (Saindelle et al., 1968; Lewis and Nicholls, 1972). Exposure to cigarette smoke causes an increase in protein-mucopolysaccharide complexes in the connective tissue of the guinea pig lung (Lupu and Velican, 1962), an increase in hydroxyproline content of the mouse lung (Rosenkrantz et al., 1969) and a change in electron spin resonance of the rabbit lung (Rowlands et al., 1967). The significance of these observations in relation to lung disease has not been elucidated.

BIBLIOGRAPHY

VII. CARDIOPULMONARY FUNCTION IN SMOKERS AND NONSMOKERS

D. PULMONARY SURFACTANT AND OTHER CONSTITUENTS

Reprint

AVIADO D M, SAMANEK M and FOLLE L E: Cardiopulmonary effects of tobacco and related substances. I. The release of histamine during inhalation of cigarette smoke and anoxemia in the heart-lung and intact dog preparation. Arch Environ Health 12: 705-11, 1966. 787

BALINT J A, BONDURANT S and KYRIAKIDES E C: Lecithin biosynthesis in cigarette smoking dogs. Arch Intern Med 127: 740-7, 1971. 788

BONDURANT S: The alveolar lining: a method of extraction; the surface tension lowering effect of cigarette smoke. J Clin Invest 39: 973-4, 1960. 789

CLEMENTS J.A: Smoking and pulmonary surfactant. New Engl J Med 286: 261-2, 1972. 790

COOK W A and WEBB W R: Surfactant in chronic smokers. Ann Thoracic Surg 2: 327-33, 1966. 791

FINLEY T N: Smoking and pulmonary macrophages. New Engl J Med 286: 789, 1972. 792

FINLEY T N and LADMAN A J: Low yield of pulmonary surfactant in cigarette smokers. New Engl J Med 286: 223-7, 1972. 793

GIAMMONA S T: Effects of cigarette smoke and plant smoke on pulmonary surfactant. Am Rev Resp Dis 96: 539-41, 1967. 794

GIAMMONA S T, TOCCI P and WEBB W R: Effects of cigarette smoke on incorporation of radioisotopically labeled palmitic acid into pulmonary surfactant and on surface activity of canine lung extracts. Am Rev Resp Dis 104: 358-67, 1971. 795

LEWIS G P, LYLE H and MILLER S: Association between elevated hepatic water-soluble protein-bound cadmium levels and chronic bronchitis and/or emphysema. Lancet 2: 1330-3, 1969. 796

LEWIS A J and NICHOLLS P J: Effect of inhaled cigarette smoke on content, release and breakdown of histamine in guinea-pig lung. Life Sciences 2: Part II, 1167-71, 1972. 797

LUPU N G and VELICAN C: Histochemistry of connective-tissue mucopolysaccharides and proteins after experimental inhalation of tobacco smoke. Azkhiv Patologii 24: 497-501, 1962. 798

MILLER D and BONDURANT S: Effects of cigarette smoke on the surface characteristics of lung extracts. Am Rev Resp Dis 85: 692-6, 1962. 799

MILLER D A, BONDURANT S, BRATTON J and MCILROY T: Effect of in vivo cigarette smoke on the surface tension of extracts of rat lungs. J Lab Clin Med 56: 929, 1960. 800

MORGAN J M: Tissue cadmium and zinc content in emphysema and bronchogenic carcinoma. J Chronic Dis 24: 107-10, 1971. 801

PRATT S A, FINLEY T N, SMITH M H and LADMAN A J: A comparison of alveolar macrophages and pulmonary surfactant (?) obtained from the lungs of human smokers and nonsmokers by endobronchial lavage. Anat Rec 163: 497-507, 1969. 802

Bibliography VII-D

Reprint

ROSENKRANTZ H, ESBER H J and SPRAGUE R: Lung hydroxyproline levels in mice exposed to cigarette smoke. Life Sci 8: 571-6, 1969. 803

ROWLANDS J R, CADENA D G and GROSS A L: Effects of tobacco smoke on lung tissue as measured by electron spin resonance. Nature 213: 1256-8, 1967. 804

SACHS D P: Smoking and pulmonary macrophages. New Engl J Med 286: 788-9, 1972. 805

SAINDELLE A, RUFF F, GUILLERM R and PARROT J-L: Libération d'histamine par la fumée de cigarette et certains de ses constituants. Rev Francaise d'Allergie 8: 137-44, 1968. 806

SEKULIC S M, HAMLIN III J T, ELLISON R G and ELLISON L T: Evaluation of five methods for the study of pulmonary surfactant. Am Rev Resp Dis 97: 131-5, 1968. 807

SZADKOWSKI D, SCHULTZE H, SCHALLER K-H and LEHNERT G: Zur okologischen Bedeutung des Schwermetallgehaltes von Zigaretten. Blei-, Cadmium- und Nickelanalysen des Tabaks sowie der Gas- und Partikelphase. Arch Hyg Bakt 153: 1-8, 1969. 808

WEBB W R, COOK W A, LANIUS J W and SHAW R R: Cigarette smoke and surfactant. Am Rev Resp Dis 95: 244-7, 1967. 809

VIII. COMMENTARY ON SELECTED ARTICLES AND THEIR PUBLICITY

VIII-A. COMMENTARY ON U.S. PUBLIC HEALTH SERVICE PUBLICATIONS

The author of this review has prepared a page by page critique of the seven documents distributed by the U.S. Public Health Service. A few examples of misquotation, omission and misinterpretation have been selected and are appended in this report. The reports have been identified by the year of their appearance. The pages pertinent in the subject of pulmonary disease are as follows:

		Reprint
(1)	1964: Smoking and Health. pp 259-315.	810
(2)	1967: The Health Consequences of Smoking. pp 87-124.	811
(3)	1968: The Health Consequences of Smoking. pp 63-86.	812
(4)	1969: The Health Consequences of Smoking. pp 35-52.	813
(5)	1971: The Health Consequences of Smoking. pp 137-230.	814
(6)	1972: The Health Consequences of Smoking. pp 35-56.	815
(7)	1973: The Health Consequences of Smoking. pp 43-91.	816

1. Change in conclusions regarding the relationship of cigarette smoking to pulmonary emphysema and chronic bronchitis (Reports 1964, 1967 and 1971).

CONCLUSIONS OF THE 1964 REPORT (59)

1. Cigarette smoking is the most important of the causes of bronchitis in the United States, and increases the risk of dying from chronic bronchitis.

2. A relationship exists between pulmonary emphysema and cigarette smoking but it has not been established that the relationship is causal. The smoking of cigarettes is associated with an increased risk of dying from pulmonary emphysema.

3. For the bulk of the population of the United States, the importance of cigarette smoking as a cause of chronic bronchopulmonary disease is much greater than that of atmospheric pollution or occupational exposures.

4. Cough, sputum production, or the two combined are consistently more frequent among cigarette smokers than among nonsmokers.

5. Cigarette smoking is associated with a reduction in ventilatory function. Among males, cigarette smokers have a greater prevalence of breathlessness than nonsmokers.

6. Cigarette smoking does not appear to cause asthma.

7. Although death certification shows that cigarette smokers have a moderately increased risk of death from influenza and pneumonia, an association of cigarette smoking and infectious diseases is not otherwise substantiated.

HIGHLIGHTS OF THE 1967 REPORT (57)

1. New data confirm and to some extent strengthen the conclusions of the Surgeon General's 1964 Report.

2. Cigarette smoking is the most important of the causes of chronic non-neoplastic bronchopulmonary diseases in the United States. It greatly increases the risk of dying not only from both chronic bronchitis but also from pulmonary emphysema.

3. Cessation of smoking is followed by a reduction in mortality from chronic bronchopulmonary disease relative to the mortality of those who continue to smoke.

4. Even relatively young cigarette smokers frequently have demonstrable respiratory symptoms and reduction in ventilatory function.

1971 SUMMARY AND CONCLUSIONS

1. Cigarette smoking is the most important cause of chronic obstructive bronchopulmonary disease in the United States. Cigarette smoking increases the risk of dying from pulmonary emphysema and chronic bronchitis. Cigarette smokers show an increased prevalence of respiratory symptoms, including cough, sputum production, and breathlessness, when compared with nonsmokers. Ventilatory function is decreased in smokers when compared with nonsmokers.

2. Cigarette smoking does not appear to be related to death from bronchial asthma although it may increase the frequency and severity of asthmatic attacks in patients already suffering from this disease.

3. The risk of developing or dying from COPD among pipe and/or cigar smokers is probably higher than that among nonsmokers while clearly less than that among cigarette smokers.

4. Ex-cigarette smokers have lower death rates from COPD than do continuing smokers. The cessation of cigarette smoking is associated with improvement in ventilatory function and with a decrease in pulmonary symptom prevalence.

5. Young, relatively asymptomatic, cigarette smokers show measurably altered ventilatory function when compared with nonsmokers of the same age.

6. For the bulk of the population of the United States, the importance of cigarette smoking as a cause of COPD is much greater than that of atmospheric pollution or occupational exposure. However, exposure to excessive atmospheric pollution or dusty occupational materials, and cigarette smoking may act jointly to produce greater COPD morbidity and mortality.

7. The results of experiments in both animals and humans have demonstrated that the inhalation of cigarette smoke is associated with acute and chronic changes in ventilatory function and pulmonary histology. Cigarette smoking has been shown to alter the mechanism of pulmonary clearance and adversely affect ciliary function.

8. Pathological studies have shown that cigarette smokers who die of diseases other than COPD have histologic changes characteristic of COPD in the bronchial tree and pulmonary parenchyma more frequently than do nonsmokers.

9. Respiratory infections are more prevalent and severe among cigarette smokers, particularly heavy smokers, than among nonsmokers.

10. Cigarette smokers appear to develop postoperative pulmonary complications more frequently than nonsmokers.

In the 1964 report, cigarette smoking is "the most important of the causes of chronic bronchitis" and for pulmonary emphysema "it has not been established that the relationship is causal."

By 1967, the two conditions were combined and cigarette smoking becomes "the most important of the causes of chronic non-neoplastic bronchopulmonary diseases."

In the latest summary, which appeared in 1971, cigarette smoking is identified as "the most important cause of chronic obstructive bronchopulmonary disease."

The change in terminology should be noted - from a separate identification of chronic bronchitis and pulmonary emphysema, finally to the all-inclusive name of chronic obstructive bronchopulmonary disease. This last term is used also for morbidity and mortality statistics, although death rates for pulmonary emphysema as distinct from chronic bronchitis are available. The reviewer is now in the process of evaluating the significance of the prevalence of bronchitis and emphysema separately.

2. Experimental proof that cigarette smoking produces pulmonary emphysema in animals. The 1967 and 1971 reports contain an adequate coverage of Auerbach's experiments.

1967 Auerbach and his associates (*5, 6*) tracheostomized 10 adult beagles and, in an attempt to approximate human smoking more closely, exposed them to cigarette smoke through the tracheostomy tube. Five dogs died during this experiment and the remaining five were sacrificed after approximately 14 months of exposure. Other beagles were kept as controls; two had tracheostomy openings. These control dogs were sacrificed at the time the last five smoking dogs were sacrificed. Lungs of the dogs exposed to cigarette smoke showed microscopically the presence of dilated air spaces, especially beneath the pleural surface. Here the alveolar septa showed a fibrous thickening of the walls with areas of rupture and dilated air sacs. Padlike attachments to alveolar septa were found. These zones of connective tissue surrounding dilated air sacs were also visible macroscopically as white areas on the lung surface. There was no thickening of the walls of small arteries and arterioles within the lung. The lungs of the control dogs were normal in appearance with none of these changes. These abnormalities approximate but are not fully concordant with some of the typical pathological findings in human emphysema. This experiment does indicate that inhaled cigarette smoke apparently can damage the pulmonary parenchyma of dogs. Other findings (*6*) as yet unpublished, indicate that abnormalities of the bronchial epithelium resulted that approximate many of the histopathologic findings of human chronic bronchitis.

A71 The investigations of Auerbach and his coworkers (*15, 16, 88*) have demonstrated by the use of both light and electron microscopy that dogs who inhale cigarette smoke through tracheostomas develop progressively more severe lesions of the bronchi and parenchyma with increased exposure to cigarette smoke. In electron microscopic studies of specimens taken from the lungs of dogs thus exposed to cigarette smoke, the following changes were observed: In 5 dogs sacrificed after only 44 days of smoking exposure, there was a proliferation of goblet cells as well as a partial loss of cilia in the lining cells, and in 5 dogs sacrificed after 420 days or more of exposure, the number of cell layers in the bronchial epithelium was found to be twice that of the nonsmoking dogs. Goblet cells and ciliated columnar cells were no longer present; instead, the surface was lined with columnar and cuboidal cells with stubby projections in place of cilia. Mitotic figures were frequently observed in the basal cells. These findings may be relevant to carcinogenesis as well as to the development of COPD.

In a long-term experiment, carried out by the same group, dogs were exposed to varying doses of cigarette smoke. Details of the experimental procedure have been outlined in the section on Pulmonary Carcinogenesis. The animals were separated into nonsmoker, filter-tip cigarette, nonfilter-light, and nonfilter-heavy exposure groups. The dogs were "smoked" for 875 days, or approximately 29 months. The animals which died during the experiment and the animals sacrificed after day 875 were examined for pulmonary parenchymal changes as well as for bronchial epithelial alterations. As seen in figures 1 and 2, dose-related pathological changes, including fibrosis and emphysema, were found in the lung parenchyma of the exposed dogs. These changes were similar to those seen in the lungs of humans with COPD.

The experiments which failed to show that cigarette smoking does not produce pulmonary emphysema have not been mentioned in the reports. Some of the work from one laboratory has been quoted to describe details that do not relate to pulmonary emphysema directly:

1968 Aviado and his co-workers (*2, 3, 4, 19, 38, 45, 46, 47, 48*) have continued their studies on bronchoconstriction and bronchodilation in animals and recently have further investigated the role of histamine in a study of inhibitors for histamine decarboxylase in rabbits, dogs, and cats (*39*). These species have variations in response to cigarette smoking as previously noted. Cats have a uniphasic bronchoconstrictor response to inhaled cigarette smoke (somewhat like man's) and dogs have a biphasic response. Rabbits were observed to behave differently than cats or dogs. Histamine has been implicated as mediating part of the bronchoconstrictive effect of cigarette smoke. The rabbit does not respond to histamine by bronchoconstriction. This study (*39*) suggests that the rabbit lacks a histamine sensitive system in the airways, in contrast to cats and dogs. Alpha-hydrazino histidine, which inhibits the enzyme histamine decarboxylase, was demonstrated to prevent much of the bronchoconstrictive effect in cats and dogs. By analogy, this suggests the possibility that histamine may mediate some of the bronchoconstrictive response to inhaled tobacco smoke noted in humans. Pretreatment with atropine has been shown to block the bronchoconstriction caused by cigarette smoke (*30*) and by histamine inhalation in humans (*7, 8, 52*).

1971 Aviado and coworkers have performed a series of experiments on live animals and in heart-lung preparations to study the effect of cigarette smoke on pulmonary physiology and structure (*18, 19, 20, 21, 22, 179, 180, 199, 200, 201, 202*). The authors observed that cigarette smoke causes acute bronchoconstriction both by the release of histamine and the stimulation of parasympathetic nerve pathways in the lung. Bronchial arterial injections of nicotine were found to cause reactions similar to those observed after cigarette smoke inhalation. The bronchoconstriction was usually followed by bronchodilatation which the authors attributed to sympathetic stimulation. As mentioned in the Chapter on Cardiovascular Diseases, nicotine has been shown to induce the release of catecholamines.

Experiments by Aviado and coworkers as well as other authors (*66, 99*) using guinea pigs showed that exposure to cigarette smoke was associated with increased bronchopulmonary resistance and decreased pulmonary compliance. The authors related these changes to the bronchoconstriction of terminal ventilatory units.

Similar experiments in dogs showed that the increase in resistance following either cigarette smoke exposure or intravenous nicotine could be blocked by pretreatment with atropine. As a parasympathetic blocker, atropine would decrease the acute bronchoconstrictive phase.

Most recently, Aviado and his colleagues (*20, 130*) have attempted to induce physiologic and anatomic changes similar to those found in the lungs of patients with emphysema. They exposed male rats to cigarette smoke, the introduction of the enzyme papain, as well as to partial tracheal ligation. In 10 rats exposed to cigarette smoke twice daily for 30 minutes over a period of 10 weeks, no changes in pulmonary compliance or resistance were noted. Also, no abnormal histological changes were observed in the group exposed only to cigarette smoke. However, animals who underwent tracheal ligation as well as smoke exposure showed increased numbers of enlarged air spaces and increased pulmonary resistance when compared with animals who underwent only tracheal ligation.

1973-Aviado and coworkers have studied the effects of hormones on the pulmonary response to cigarette smoke inhalation and intravenous nicotine injection. Subcutaneous progesterone administration, prior to nicotine or smoke exposure, reduced the bronchoconstrictor response in rats (*64*). A similar experiment involving pretreatment of dogs with glucocorticoids resulted in variable bronchoconstrictor responses after exposure to cigarette smoke (*12*).

In the 1971 quotation, there is no mention that the attempt to induce emphysema in rats by exposure to cigarette smoke failed, although other procedures caused the lesions. The failure to elicit emphysema appeared in the conclusions of two articles which the documents overlooked.

Summary of Ito and Aviado (1968)

Rats exposed to cigarette smoke daily for ten weeks did not develop signs of pulmonary emphysema. The rats subjected to experimental ligation of the trachea and intratracheal injection of papain developed signs of pulmonary emphysema but exposure to cigarette smoke did not uniformly influence the various signs. Functional residual capacity was not markedly elevated although histological examination showed a higher percentage of air spaces in emphysematous rats exposed to cigarette smoke. Cigarette smoke caused an increase in pulmonary resistance only in the rats with experimental emphysema. The increase in resistance is interpreted to mean an increase in bronchomotor tone. Isoproterenol injection induces bronchodilatation, more intensely in rats exposed to cigarette smoke.

Summary of Aviado et al. (1970)

This is the second reported attempt to demonstrate that cigarette smoke can induce pulmonary emphysema in rats. The negative results have been scrutinized to determine the significance of the changes in airway resistance and content of biogenic amines during exposure to cigarette smoke. These changes in the lung are not important in determining the appearance or disappearance of pulmonary emphysema in rats. In the same animal species, tracheal ligation and endotracheal injection of papain produce pulmonary emphysema.

3. Evaluation of air pollution. The U.S. Public Health documents have arrived at the conclusion that cigarette smoking is the most important factor in the causation of chronic bronchitis and pulmonary emphysema. They have interpreted articles relating to air pollution and industrial hazards as indicating that these are less important than cigarette smoking. A re-examination of 48 articles indicates just the opposite conclusion made by the authors and details are outlined in Sections III and IV. One example is the report of Phelps and Koike (1962). The 1964 report has the following citation:

> In the "Tokyo-Yokohama Asthma" studies, a severe asthma-like disease, presumed to be caused by air pollution, affected cigarette smokers predominantly (155). The absence of smoking data on unaffected members of the same population leaves the question of an additive effect of cigarette smoking unanswered. One study suggests that non-smokers may have a slightly greater prevalence of asthma than smokers; the possibility of bias due to self-selection of the base population could not, however, be excluded in this study (84).

Phelps and Koike concluded that air pollution is the cause of the disability. Removing the patients from the area caused a dramatic relief. The quotations are as follows:

> As the disease progresses (usually in the patient with symptoms who remains in this area for several years or who returns to the area after having had the disease during a previous tour), more shortness of breath is manifested. The patient by this time is usually receiving adrenal steroids and has been frequently hospitalized. It is at this time that all of the symptoms and signs of emphysema are present. This is more likely to occur in persons who are heavy cigarette smokers. Although the study is by no means complete, it is believed that there is evidence that air pollution, of unknown content, is the cause of much disability which, under certain conditions, may progress rapidly to emphysema.
>
> The follow-up studies revealed that those patients who were transferred to the United States early in the course of the disease had dramatic relief of their symptoms. All pulmonary function studies returned to normal within one to two months after the arrival of these patients in the United States. Their function studies took longer to return to normal than their symptoms. Those persons who had their disease for a long period of time (two to three years) took much longer to become asymptomatic, and it took even longer for their pulmonary function studies to become normal. Most of the patients were improved so far as coughing and wheezing were concerned, but they still had shortness of breath. The first sign of recovery appeared to be an increased response to IPPB with Isuprel.

VIII-B. COMMENTARY OF SELECTED ARTICLES

The conclusions of the U.S. Public Health Service Publications have been accepted by several organizations, government bodies and authors. Quotations from the following articles have been selected to illustrate the manner by which the conclusions have been quoted for special purposes. The articles are arranged according to the year of their publication.

Bibliography VIII-B

Page			Reprint
180	(24)	SCHUMAN L M: Epidemiology of smoking related diseases which physicians encounter in their office practice. Dis Chest 54: 176-9, 1968.	833
181	(25)	JACOBS E C: Smoking - insidious suicide and personal air pollution. Military Med 135:678-81, 1970.	834
182	(26)	BENNETT J S: Smoking - time to practice what we preach. Canad Med Assoc J 106:276, 278, 1972.	835

(8) FIESER L F : More on smoking and health. Chemistry 19: , 1964.

You may have seen headlines about the report of the Surgeon General's Advisory Committee on Smoking and Health (Chemistry, February 1964, page 2), but I doubt that you have waded through the 387-page document or the lengthy newspaper accounts of its findings. Since I was the only chemist on the 10-man advisory committee, I could hardly decline a request from the editor of Chemistry for a summary of the report addressed to Chemistry's readers. You may care to know what it all boils down to, so that you can make a wise decision for yourself and so that you can offer sound advice to others.

Countless weekend committee meetings were held in Washington in which we worked over a Friday-Saturday-Sunday stretch, continuing each day from 8:30 a.m. to about 8 p.m. One problem was that the medical men, who properly predominated on the committee, would not use a simple term such as "cancer of the mouth" when the more dignified medical term "carcinoma of the buccal cavity" was available.

The unanimous opinion of our committee was: "Cigaret smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action."

A few of the findings on which this judgement was based are as follows:

- *Cigaret smoking is causally related to lung cancer in men; the magnitude of the effect of cigaret smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction.*
- *The risk of developing lung cancer increases with duration of smoking and the number of cigarets smoked per day and is diminished by discontinuing smoking.*
- *Cigaret smoking is the most important of the causes of chronic bronchitis and increases the risk of dying from chronic bronchitis and from pulmonary emphysema.*
- *Male cigaret smokers have a higher death rate from coronary artery disease than nonsmoking males.*
- *The death rate for smokers of cigarets is about 70% higher than that for nonsmokers.*

These are strong words and they call for strong actions. It is not yet clear what remedial actions will be instituted by governmental agencies, but there is no question about the course young people should take. Don't smoke cigarets. Don't let yourself fall into the habit of smoking. It is a habit which many people regret but find difficult to break. You young people are in a position to make a decision in advance and so save yourselves from concern about remedial measures at a later, critical stage.

Commentary (8) Fieser, Cont.

The author of this Editorial has combined the two pulmonary diseases to read "increases the risk of dying from chronic bronchitis and from pulmonary emphysema." In the 1964 statement, the two diseases were covered in separate sentences: "cigarette smoking is the most important of the causes of chronic bronchitis" and "a relationship exists between pulmonary emphysema and cigarette smoking but it has not been established that the relationship is causal."

(9) KAMPMEIER R H: Smoking and noncancerous pulmonary disease. Southern Med J 57: 981-3, 1964.

Though there have been numerous demonstrations of impairment of pulmonary function in heavy cigarette smokers as compared to control groups, the main evidence of the hazard of cigarette smoking in terms of chronic bronchitis and eventual emphysema comes from epidemiologic studies. Everyone recognizes that air pollution, in cities especially and in certain occupations, can not be divorced from inhaled cigarette smoke when considering the ill effects of inspired air. Yet, other than asthma and familial tendencies to emphysema, chronic cough and infection are accepted as important factors in the development of emphysema. No one denies the "smokers' cough" and few would deny the airway resistance which is part of inhaled smoke, both unquestioned potentials in the development of emphysema. The pathologic evidence of alterations in the bronchial mucosa in prolonged cigarette smoking is so overwhelming that few argue about this anymore. The symptoms of this chronic bronchitis as a role in emphysema need no more than a mention.

What it all adds up to, is that no one has been able to show unquestioned causal relationship between cigarette smoking and chronic bronchitis and/or emphysema even approaching that of its relationship to bronchogenic carcinoma. But no matter how good a case the apologist for tobacco may make for chronic infection and air pollutants other than cigarette smoke as a cause for bronchitis and for emphysema, the fact remains that cigarette smoke is a pollutant which in its own right can impair pulmonary function and therefore has a deleterious effect on pulmonary structures over and above the other unavoidable factors in the air of our environment and the bacterial flora of our respiratory tract. It would be rather nonsensical to discard as accidental increased mortality rates in heavy cigarette smokers over those of control groups of nonsmokers in epidemiologic studies of chronic bronchitis and emphysema.

The application of epidemiologic studies to pulmonary emphysema and chronic bronchitis is mixed up with pathologic evidence. The prevalence of respiratory symptoms does not refer to incidence of these two separate disease entities. Although the 1964 statement has made a distinction between the influence of cigarette smoking to symptoms of bronchitis, others have interpreted the symptoms as indicating the positive presence of the disease.

(10) EDITORIAL. West Virginia Med J 60: 51-2, 1964.

> An association between cigarette smoking and chronic lung disease has been established beyond medical argument. Cigarette smoking accounts for the majority of cases of emphysema and emphysema deaths now outnumber tuberculosis deaths. It has been estimated that smoking ten cigarettes per day will lead to a diminution of four years in life expectancy for the average American. Cancer of the lung is from 20 to 30 times more prevalent in the cigarette smoker than the nonsmoker. This is our most deadly cancer with a salvage rate of only 5 per cent. A study of British physicians shows that at age 35 the chances of dying within the next ten years are 1-23 for the heavy cigarette smoker and 1-90 for the nonsmoker.

The opening sentence refers to association between cigarette smoking and chronic lung disease but the second setence condemns smoking because it accounts for the majority of cases of emphysema. A causal relationship between cigarette smoking and emphysema has not been established, according to the 1964 report.

(11) RAVENHOLT R T : Cigarette smoking: magnitude of the hazard. Am J Public Health 54: 1923-26, 1964.

The censensus of findings of many studies[9] indicate that approximately nine-tenths of lung cancer deaths in the United States today are caused by smoking; and this consistent fact may be used in conjunction with the above findings (Table 1) to achieve a rough measure of total tobacco disease mortality:

Deaths from lung cancer in total population	122	1
Excess deaths from all causes among smokers	723	6

Hence, excess mortality from all causes among smokers in an American-type population is probably about six times greater than total lung cancer mortality in that population.

During 1962, 41,376 deaths were ascribed to lung cancer in the United States[10]; and by application of the lung cancer index of one-sixth, one can estimate that there were roughly a quarter million excess deaths due to smoking—which was 14 per cent of all deaths (1,756,720) from all causes. The relative importance of tobacco (especially cigarettes) as a hazard to life in the United States is indicated by the following balance of causes of death. (Figure 1.) The sum of all deaths from *accidents, infection, suicide, homicide, alcohol,* and *stomach cancer* only equals the quarter-million deaths from tobacco disease in the United States during 1962.

American Balance of Hazards to Life, 1962

Quarter Million Deaths from Tobacco	
*Lung Cancer	37,000
†Other Cancer Deaths (Of larynx, bladder, etc.)	23,000
‡Coronary Disease	119,000
‡Other Vascular Disease (Strokes, etc.)	35,000
‡Other Tobacco Diseases (Emphysema, bronchitis, etc.)	36,000

Quarter Million Deaths from Selected Causes	
All Accidents	97,139
Motor vehicle	40,804
Aircraft	1,254
Drowning	5,161
Other accidents	49,920
All Infectious Diseases	93,745
Tuberculosis	9,506
Pneumonia	66,999
Typhoid	15
Diphtheria	41
Other Infections	17,184
Suicide	20,207
Homicide	9,013
Alcohol	9,959
Stomach Cancer	19,378

* Nine-tenths of all (41,376) lung cancer deaths. † Number estimated from lung cancer index. (Total coronary disease deaths—527,581; total deaths from all causes—1,756,720.)

This article illustrates how portions of the 1964 statement has been used to equalize "excess death among smokers" with hazards to life. The death rate from emphysema and bronchitis is multiplied by lung cancer index and those compared with deaths from selected causes.

(21) HUTCHISON G B : The nature of epidemiologic evidence: smoking and health. Bull NY Acad Med 44: 1471-5, 1968.

Epidemiologic Evidence

An extensive literature on associations between smoking and cardiovascular disease is now available. I propose to comment on some of the studies in this literature in which the unit of observation is a person and in which information is collected to characterize persons as to state of health. These are the studies which are commonly referred to as epidemiologic studies. When these studies are interpreted in terms of cause-effect relations the cause-effect concept is usually the pragmatic one.

The proof of cause-effect would be established or rejected by deliberately manipulating the smoking habits of such persons and observing the results. No such studies have been made to my knowledge. Controversy, when it occurs, rests on differences of opinion as to what constitutes proof in the absence of such a manipulative study. There are those who feel that proof is *never* established without such human experimentation. Others feel that proof can be established through observational studies, but there is little agreement as to what sorts of observations are required.

A number of schemes have been suggested for assuring such proof. Koch's postulates are an early attempt, but are applicable only when the causative event is exposure or nonexposure to living organisms. The surgeon general's committee has proposed a number of conditions which must be satisfied. These include consistency, strength, specificity, and coherence of the association. The ultimate decision, however, is said to be judgmental.

The discussion of epidemiology is followed by the conclusion that the evidence is adequate to support the cause and effect relationship between lung cancer and cigarette smoking. If the same principle is applied to pulmonary emphysema, a cause and effect relationship has not been established.

(22) NYLAN L H : Air pollution and emphysema: Connecticut Med 32: 706-7, 1968.

About 20,000 Americans will die of emphysema this year, seven times the number that succumbed to it a decade ago. It disables one out of fourteen American workers over forty-five years of age. E. Cyler Hammond,[1] Vice President of the American Cancer Society told a senate subcommittee that a recent study of 120,000 men indicates that a combined atmosphere of cigarette smoke and occupational pollution creates heigthened risk of emphysema. A nonsmoker exposed to occupational pollution (smog, pollen, dust, exhaust fumes or other irritants) has one chance in ninety of developing emphysema. Among heavy smokers exposed to the same air pollution, one in seven develops this crippling disease. These findings are not new and are supported by those of others that air pollution and cigarette smoking often leads to destruction of lung tissue that characterizes emphysema.

The risk of smoker exposed to air pollution cited by Hammond in his testimony is one of 10 possible figures. The other reports do not indicate such a disparity between smokers and nonsmokers.

(23) OCHSNER A : Prevention of executive obsolescence. J Am Geriatrics Soc 16: 1077-82, 1968.

> Severe emphysema is a condition that can be considered worse than cancer. The patient with cancer of the lung either dies (only about 6 per cent can be cured) or gets well, whereas the patient with severe emphysema has a living death. According to the United States Public Health statistics, more than 12 million people in the United States today are completely disabled by severe emphysema caused directly by cigarette smoking. In 1965 in the United States, there were 77 million man-days lost from work because of tobacco, an additional 88 million man-days of sickness in bed as the result of use of tobacco, and 360,000,000 man-days of restricted activity because of the effects of tobacco. On the basis of these statistics, and using minimal figures of $40 a day for those totally disabled and $20 a day for those partially disabled, the loss of income from disability caused by tobacco in 1965 amounted to $15,800,000,000. The only reason that tobacco does not cause senescence more often is that frequently it causes early death—the dubious advantage of being spared early obsolescence.

The Surgeon General's report has been used to discuss tobacco and senescence. The author, a foremost surgeon, has accepted all the statistics and figures in 1967 document.

(24) SCHUMAN L M : Epidemiology of smoking related diseases which physicians encounter in their office practice. Dis Chest 54: 176-9, 1968.

Chronic bronchopulmonary diseases were cau
ly implicated in the 1964 Advisory Committee
port to the Surgeon General. The evidence w
deemed adequate for a causal relationship betw
cigarette smoking and chronic bronchitis and
was strongly implicated as increasing the risk
death from pulmonary emphysema. Despite
recent attempts at more precise definitions of chr
ic bronchitis and pulmonary emphysema, the sta
of such definitions over the immediate past in
own country and those in other countries mak
trends and comparisons difficult if we attempt
separate the two entities. Thus, mortality and m
bility analyses are better applied to a combination
of the two—chronic bronchitis and/or emphysema.
As a problem in *mortality*, chronic bronchitis and/
or emphysema presently claim half as many deaths
as does lung cancer. However, in the 16-year peri-
od, 1950–65, deaths from these two non-neoplastic
pulmonary diseases have increased over six-fold
from 3,157 deaths reported in 1950 to 23,432 re-
ported in 1965.[4,5] This increase has been greater
than the similarly appalling toll from lung cancer.
The most dramatic rise has been for the emphy-
sema component for which the age-adjusted mor-
tality rates rose from 1.3 per 100,000 in 1950 to al-
most 13.0 in 1965. Deaths from chronic bronchitis
rose less spectacularly, only doubling in the same
period. Although some of these increases must
represent diagnostic improvement, it is difficult to
ascertain the degree to which this operated. The
causal relationship with cigarette smoking and the
use of cigarettes in this period would suggest that
a major part of this rise in mortality must be real.

The explanation for combination of chronic bronchitis and emphysema in mortality statistics is not a convincing one. Since 1964, the diagnosis of the two disease entities has advanced to the point of widespread application. It would be reasonable to analyze the death rates from the two diseases separately.

(12) WAKERLIN G E : Cigarette smoking and the role of the physician. Circulation 29: 651-6, 1964.

Smoking and Other Diseases

Epidemiologic, experimental, and clinical studies have demonstrated adverse relationships between cigarette smoking and lung cancer, chronic bronchitis, and emphysema. One of the complications of emphysema is cor pulmonale. Cigarette smoking has also been shown to be associated with an increased incidence of arteriosclerosis of the pulmonary arterioles and small arteries.

Increased morbidity and mortality among cigarette smokers have been reported for certain other forms of cancer and for peptic ulcer.

Smoking and Over-all Death Rates

Cigarette smokers show adverse changes in structure and function of the lungs and bronchial tree.[18, 19] Pulmonary function changes include decreased vital capacity and decreased forced expiratory volume.[20] Some of these changes revert toward normal in those who stop smoking.[21]

In addition to the greater risk of illness and death from disease, recent studies suggest a reduced sense of well-being among cigarette smokers. Thus, compared with absence of the cigarette habit, cigarette smoking is more frequently associated with cough, shortness of breath, decreased appetite, and increased "nervous tension."[22] An adverse association of cigarette smoking with body function appears to begin with fetal life, since more premature infants are born to mothers who smoke cigarettes.[23, 24]

Recent Actions with Reference to Smoking

The statements are individually accurate. The implication to the reader is unavoidable: pulmonary effects of cigarette smoking is responsible for deaths which in turn has led to recent actions against smoking.

(13) FISHBEIM M : Medical progress in 1964.

> The rise in cancer of the lung was associated with a considerable increase in emphysema in many parts of the world, particularly in the U.S., Canada, and England. One survey indicated that about 25% of men over 45 have some degree of emphysema. The condition is from seven to 13 times more frequent among cigarette smokers than among nonsmokers. Both cigarettes and air pollution have been considered as causative factors. Great attention is now focused on determining the exact relationships among these factors and diseases.

> Looking back at 1964, a few peaks of interest become apparent in each area of medical research and medical practice. Heart disease, cancer, and high blood pressure with stroke received major medical attention as the leading causes of death. Infectious diseases were controllable as never before, and more of the infectious diseases of childhood became wholly amenable to prevention and cure.

The survey showing that 25% of men over 45 have some degree of emphysema refers to prevalence of coughing and expectoration. The quoted 7 to 13 times more frequent among cigarette smokers is also based on incidence of respiratory symptoms. The mortality ratio for pulmonary emphysema among smokers compared to nonsmokers is about 3 times.

(14) U. S. Department of Health, Education and Welfare. Public Health Service Publication 1103-F: 1-2, 1965.

SURGEON GENERAL'S COMMITTEE

By 1962 scientific research had implicated the cigarette in several major diseases. In addition to chronic bronchitis and emphysema, these included heart disease and lung cancer. That year, the Surgeon General of the Public Health Service appointed an advisory committee of 10 eminent scientists to review the accumulated evidence. The committee had advice and consultation from nearly 200 specialists representing every related field of interest.

THREE KINDS OF EVIDENCE

The Surgeon General's Committee reviewed three kinds of research evidence.

1. Animal Experiments

Animals exposed to tobacco smoke show severe damage to the cells lining the air tubes—the same kind of damage seen in heavy smokers. (A pack a day or more is considered "heavy smoking.")

2. Human Tissue

When the cells of the bronchi of smokers and nonsmokers are compared, the smokers' cells show characteristic damage: loss of the cilia and irregular shapes. These changes have been noted in thousands of studies, both in living patients and at autopsy.

3. Population Studies

Extensive and repeated studies of large numbers of people have consistently shown that cigarette smokers are more likely to have symptoms of respiratory disease than nonsmokers. They cough more, bring up more phlegm, and complain more of breathlessness.

SMOKING AND HEALTH REPORT

In January 1964, the Surgeon General's Committee finished the most comprehensive study of smoking and health ever undertaken. Studies involving more than a million men had been reviewed. For cigarette smokers, the death rate from chronic bronchitis and emphysema was found to be *six times* greater than for nonsmokers. A 500-percent difference! Ex-smokers had a death rate from these diseases about 40 percent greater than for nonsmokers. Men who began smoking before the age 20 had a higher death rate than those who started later.

Commentary (14) U.S. Department of Health, Education and Welfare, Cont.

This widely distributed leaflet contains selected statements, each one quoted from the 1964 report. The combination of the three kinds of evidence do not relate to chronic bronchitis or pulmonary emphysema mentioned above and below the quotation. The animals were not sick with emphysema or bronchitis, the human tissue was obtained from smokers who were not suffering from emphysema or bronchitis, and the population studies surveyed respiratory symptoms which do not necessarily signify emphysema or bronchitis.

(15) FOGARTY J E : Delivered to the Task Force on chronic bronchitis and emphysema. NTA Bulletin 3-6, 1967.

> What is the cause—or should I say causes—of emphysema, the condition that begins innocently enough with a mild cough and seems to proceed to increasing shortness of breath until the normal activities of the day become increasingly burdensome?
>
> Is cigarette smoking a factor? We are told in the report of the Surgeon General's Advisory Committee on Smoking and Health that cigarette smoking is an important cause of chronic bronchitis and that a "relationship" exists between cigarette smoking and emphysema. Has that relationship as yet been defined? Despite the accumulating evidence that cigarette smoking and emphysema are intimately linked, our society is heedlessly smoking six per cent more cigarettes a year than in 1964, when the report of the Surgeon General's committee was released.
>
> What about air pollution? In all honesty, we do not need experts to tell us that air pollution is an insult to our respiratory tract, yet until now our national complacency has permitted the continued spewing of poisons into the air.

The relationship of cigarette smoking to chronic bronchitis and pulmonary emphysema is differentiated in this article, according to the 1964 report. The term cause is unfortunate; risk factor would have been more appropriate.

(16) SHAMBAUGH G E : Additional data on smoking. Arch Otolaryng 85: 589-90, 1967.

THE NATIONAL Center for Health Statistics in October 1966 published the Mortality Statistics From Diseases Associated With Smoking, from 1950 to 1964. Two groups of diseases are considered: those *causally related* to smoking, namely cancer of the lung, cancer of the larynx, cancer of the lip, and chronic bronchitis, and those *associated* with smoking but where the evidence is not yet sufficient to establish a causal relationship. The latter group comprises arteriosclerotic heart disease including coronary disease, cirrhosis of the liver, emphysema, ulcer of the stomach, cancer of the esophagus, cancer of the oral cavity other than the lip, cancer of the bladder and other urinary organs, and noncoronary cardiovascular disease. *JAMA* (199:24 [Jan 23] 1967) carries an interesting study of cigarette smoking in dogs. After more than 420 days of smoking through a tracheostomy tube there was marked cardiac enlargement compared to controls, and pulmonary fibrosis and emphysema in all the smoking dogs, not found in any of the controls. Interestingly some of the dogs showed a liking of cigarette smoking as indicated by tail-wagging and jumping into the smoking box voluntarily. With this evidence perhaps emphysema should be reclassified as causally related to smoking, rather than associated with smoking.

The widely publicized "smoking dogs" has undoubtedly led to the reversal of the statement from no causal to causal relationship between cigarette smoking and pulmonary emphysema. There are other attempts in animals which failed to show a cause and effect relationship but these were never publicized.

(17) WHATLEY J L : Battle for breath. Today's Health 42-71, 1967.

Emphysema and chronic bronchitis are the fastest rising causes of death in the country. Almost 20,000 people will die this year from emphysema or its complications. Whether this increase is due to better methods of diagnosis, or to the greater longevity of our population, we do not know. Certainly, part of the increase is due to modern environmental conditions (exhaust fumes, smog, cigarette smoke, etc.).

Emphysema is about 13 times more prevalent among cigarette smokers than among non-smokers, but many who have *never* smoked contract the disease. Men develop emphysema five to 10 times more frequently than women, probably because women are "abdominal breathers" (they use the diaphragm and abdominal muscles more), whereas men are "chest breathers" (they use the chest muscles more).

At present, we don't know the exact cause of pulmonary emphysema, but we do know quite a bit about it. We know that it is an overinflation of the lung due to loss of that organ's natural elasticity. The smaller airways (bronchial tubes) narrow from spasm, irritation, infection, or a combination of the three. This narrowing traps the air in the small air sacs (alveoli), and they dilate and lose their elasticity, or ability to recoil.

The 13 times prevalence of emphysema among cigarette smokers is based on incidence of respiratory symptoms which does not necessarily signify the disease. The author avoids stating that emphysema is caused by cigarette smoking. Even though the author does not know the exact cause of pulmonary emphysema, the hurried reader will undoubtedly regard the 13 times prevalence of cigarette smoking as a causative factor.

(18) ABELSON P H : Changing attitudes toward smoking. Science 161: 319, 1968.

The attitudes of the people of the United States toward cigarette smoking are undergoing a major change. In the 30-year period prior to 1964, per capita consumption of cigarettes tripled. During the last 4 years, per capita consumption of cigarettes has leveled off, and currently it may be dropping. The 1964 Surgeon General's Advisory Committee report entitled "Smoking and Health" was a major milestone. The report set in motion developments that ultimately will have a profound effect. One consequence was the stimulation of research bearing upon the effects of smoking. A recent compendium lists 364 projects in 36 states, the District of Columbia, and 25 foreign countries.

Out of this research activity has come substantial evidence that the effects of smoking are even more serious than was stated in the 1964 report. Highlights of the findings have been presented in a new U.S. Public Health Service document.* The most striking finding is that "the life expectancy for a two-pack a day, or more, smoker at age 25 is 8.3 years less than [that for] the corresponding non-smoker."

The 1964 report probably has influenced the smoking habits of physicians. At one time many of them were heavy smokers. A recent survey† indicates that 100,000 physicians have stopped smoking cigarettes. Of all the physicians surveyed, 35 percent had never smoked, 36 percent had smoked at one time but had stopped, and only 29 percent were still smoking. In contrast, 52 percent of the general adult male population currently smoke cigarettes.

The survey also indicates that physicians are deeply concerned over the effects of smoking. More than 90 percent stated that they associate smoking with chronic bronchitis, lung cancer, and emphysema, and almost as many associate it with peripheral vascular disease and coronary artery disease. The responses of physicians who have stopped smoking are revealing. When asked on the survey questionnaire why they stopped, 60 percent checked "Protect my future health," 47 percent checked "Occurrence of certain symptoms," and 43 percent checked "Scientific reports convinced me."

Following the appearance of 1967 Report, a second wave of Editorials appeared. The smoking habits of physicians are discussed here. It is important to point out that 43% who stopped smoking were convinced of the scientific reports summarized in the U. S. Public Health documents.

(19) DELARUE N C : Health hazards of smoking. Modern Med Canada 23: 37-42, 1968.

> 2. *Chronic Bronchitis and Emphysema.*
> There are now 80,000 annual deaths in the United States from these diseases and although they both may develop in non-smokers, the risk of death in cigarette smokers is increased from eight to 15 times as compared to the non-smoking population. In the five-year period between 1959 and 1964 deaths from chronic bronchitis increased 90 per cent and over the same period, deaths from emphysema increased 104 per cent. There were 421,000 new cases of bronchitis recorded in 1965, and 267,000 new cases of emphysema defined in the same period. At that time, it was estimated that there were more than three million cases of chronic bronchitis in the United States.

This special article appeared in a Canadian journal. It can be noted that United States statistics are quoted here, even though there is information directly from Canada. Other countries have relied on the U. S. Public Health documents for statistics relating to chronic bronchitis, although its incidence varies from country to country.

(20) HARKEN D E : Smoking . . . The Masochistic massacre. Dis Chest 54: 445-9, 1968.

The combination of seven prospective studies reveals that the mortality rates of cigarette smokers over non-smokers for all causes of death was 7 per cent higher in smokers.

Let us look at some cold facts on mortality in a combination of seven prospective mortality records of smokers versus non-smokers:

Cancer of lung	(10.8)	1000 per cent (leading cancer in men)
Bronchitis and emphysema	(6.1)	600 per cent (and leading cause of disability)
Cancer of the larynx	(5.4)	
Oral cancer	(4.1)	
Cancer of the esophagus	(3.4)	
Peptic ulcer	(2.7)	
Atherosclerotic disease	(2.6)	
Coronary artery disease	(1.7)	70 per cent

Although death rates of chronic bronchitis separately from pulmonary emphysema are available, the 1967 report combines the two diseases, presumably to improve the statistical significance. Reference to the mortality ratio for smokers to nonsmokers appearing in articles such as the one under consideration do not question the practice.

(25) JACOBS E C : Smoking: insidious suicide and personal air pollution. Military Med 135: 678-81, 1970.

Facts

Smoking remains the foremost preventable cause of disease, disability and death in the United States.[8-13] Smoking causes coronary artery disease, lung cancer, emphysema, thrombo-angiitis obliterans and the like, annually producing hundreds of thousands of premature deaths and many hundreds of thousands of cripples. Tobacco diseases are causing many millions of man-days lost annually in this country. Tobacco diseases can shorten the smoker's life by eight or more years,[12] can cause a death every 1.5 minutes,[15] and cost the Nation between $4 billion[9] and $20 billion annually.[13]

The statements in the U. S. Public Health documents are abbreviated in this short paragraph. It can be noted that smoking is stated to cause pulmonary emphysema. The phrase "no causal relationship has not been established" has been omitted.

(26) BENNETT J S : Smoking: time to practice what we preach. Canad Med Assoc J 106: 276, 278 1972.

The 1962 report on Smoking and Health by the Royal College of Physicians (London) was discounted by the tobacco industry as contributing little but "statistical association". The College's new report "Smoking and Health Now" (1971) points out that the criticism of "statistical evidence only" cannot be upheld as a valid objection. Much of aetiology, morbidity incidence, etc., on human disease is based on statistical evidence; the pro-smoking faction suggests that, as far as smoking is concerned, no laboratory evidence is available to show its responsibility for lung cancer. However, the recent work of Auerbach and Hammond on invasive lung cancer in dogs should convince the Doubting Thomas. Statements from the U.S. Department of Health, Education and Welfare (1971) are:

1. Cigarette smoking is the major cause of lung cancer.
2. Cigarette smoking is the most important cause of chronic obstructive broncho-pulmonary disease, principally chronic bronchitis and pulmonary emphysema.
3. Cigarette smoking is an important risk factor in the development of coronary heart disease and, by accelerating damage already present as a result of coronary heart disease, may contribute to sudden death.

Isn't it time that the medical profession became a little more active in the efforts to reduce one of the major health hazards of our time. We tend to get worked up about pollution but do little about one of the greatest contaminants of all — the tobacco smoker.

The 1971 U. S. Public Health document and the 1971 report from the Royal College of Physicians are cited in this article. The widely publicized smoking dogs are cited as the most important laboratory evidence to support the statement that cigarette smoking is the major cause of lung cancer and the most important cause of chronic bronchitis and pulmonary emphysema.

VIII-C. PUBLICITY RELATING TO SMOKING AND HEALTH

The widespread distribution of the seven documents on "Smoking and Health" has led to the appearance of secondary publications. Almost all of them accept the conclusions appearing in the seven documents that cigarette smoking is the most important cause of chronic bronchitis and pulmonary emphysema. A few articles contest the statement but none has appeared in recent years. The articles are listed in the following order:

BIBLIOGRAPHY

VIII-C-(1). ARTICLES AND PUBLICITY FAVORING SURGEON GENERAL'S STATEMENT

	Reprint
American Cancer Society: 1968 cancer facts and figures. pp 1-32, 1967.	836
ANON: Answers to cigarettes quiz.	837
ANON: U.S. report reaffirms cigarets are hazardous.	838
ANON: Women face hazards of smoking. p. 44	839
ANON: World conference on smoking.	840
BECKERMAN S C: The health consequences of smoking. J Maine Med Assoc 58: 222, 1967.	841
BERITIC T: Pusenje, bolest i zdravstveno prosvjecivanje. Lijec Vjesn 86: 1409-11, 1964.	842
British Medical Journal: Menace of smoking. Br Med J 3: 753-54, 1967.	843
British Medical Journal: The smoking disease. 1 (5740):61-62, 1971.	844
BROWNING R H: The physician and the cigarette. Education concerning dangers of smoking essential to render habit socially unacceptable. RI Med J 50: 735-56, 1967.	845
Bulletin of the Los Angeles County Medical Association: The health consequences of smoking. A public health review: 1967. Bull Los Angeles Co Med Assoc 98: 1-2, 57-58, 1968.	846
CRALLEY L J: Presidents page. Am Ind Hyg Assoc J 30: 2, 1969.	847
DAVIS H L: Current facts concerning smoking and pulmonary disease and cardiovascular disorders. Memphis Mid-South Med J 73-75, 1966.	848
DEODHAR S D: Smoking and health. Indian J Med Sci 26: 327-37, 1972.	849
DIEHL H S: Cancer 110.	850
DIEHL H S: Opportunity unlimited. Min Med 699-701, 1969.	851
DOYLE J T: Tobacco and heart disease. Postgrad Med 44: 188-92, 1968.	852
El Dia Medico: La costumbre de fumar. El Dia Med. 265, 1967.	853
EVANG K: Sigarettoyking og helse. Pp 300-4, 1964.	854
EVANG K: Tupakointi terveyden vaarana. Suom Laakarilehti 24: 3108-11, 1969.	855
FLETCHER C M: Cigarettes and respiratory disease. NTRDA Bull 12-14, 1968.	856

FLETCHER C M: Cigarettes and respiratory disease. Inhalation Ther 14: 45-50, 1969. 857

GARCIA ECHEVERRIA J P: Algo mas sobre el habito de fumar. pp 1563-66. 858

GODBER G: The case against smoking. pp 20-25. 859

GUTHRIE E H: Smoking and health....one year late. J Sch Health 53-57. 860

HAMMOND E C: The multiple health hazards of cigarette smoking. Presented at: 92nd Annual Meeting of the American Public Healt Association. pp 1-26, 1964. 861

HAMMOND E C, BERGLUND L and KASLOW R: Smoking habits and disease. Minn Med 44. 862

HOFFMANN F P: Smoking 110-11, 1967. 863

Journal of Iowa Medical Society: The month in Washington. J Iowa Med Soc 58: 918, 21, 1968. 864

KOLLER S: Lebensverkurzung durch lungenkrebs und kreislaufschaden als folge des zigarettenrauchens. DA 4: 191-206, 1968. 865

LISTER J: Smoking and health now. N Engl J Med 284: 656-57, 1971. 866

LUNDAR J: Tobakksroking og lungesykdommer. Tidsskr Nor Laegeforen 85: 437-42, 1965. 867

McMILLEN S I: Coronary and cancer by the carton. In: Cancer by the Carton. Fleming H Revell Company: Westwood, NJ pp 11-22. 868

McMILLEN S I: The case against cigarettes: some summaries. In: Cancer by the Carton. Fleming H Revell Company: Westwood NJ pp 42-59. 869

Medical News: Emphysema and smoking link -- new evidence. Med News 1969. 870

Medical Tribune: Dr. Terry warns of cigarette danger. 871

Medical Tribune: Women smokers: effects near those in men or greater. Med Tribune 13 (7): 1, 24, 1972. 872

Medical Tribune: W. Coast survey of doctors shows 39% still smoke. 873

Medical World News: How goes the war on smoking? Med World News 46-51, 1969. 874

Medical World News: PHS heats up warfare on smoking. Med World News 29-30, 1967. 875

Medicina: Salud y tabaco. Medicina 28: 413-14, 1968. 876

MERRILL M H: States take action to combat smoking. Johper 10, 1965. 877

MEURMAN L: Tobaksronkning -- forgiftning eller stimulans? 756-64. 878

MURRAY D: Our fastest-growing health menace. Readers Digest 90: 111-14, 1967. 879

OCHSNER A: Health hazards from tobacco. 267-81. 880

PHILLIPS A J: The relationship between smoking and health -- a review of the evidence. Can J Public Health 55: 12-15, 1964. 881

POPPIUS H: Klinisktfysiologiska studier. Lakartidningen 67: 397-401, 1970. 882

Public Health (London): Special report: eight years after. Public Health 85: 133-36, 1971. 883

RANDHAW I H: Smoking and its injurious effects on health. 13: 187-93, 1963. 884

RASTELLI M: Tabacco e salute. Clin Ter 49: 85, 1969. 885

ROSENBLUM L: Experts discuss smoking. 14, 1964. 886

Royal Society of Health Journal: Smoking and health now. R Soc Health J 91: , 1971. 887

SCOTT R B and WALKER R M: Smoking and respiratory disease. In: The Medical Annual, John Wright and Sons Ltd, Bristol, 1965, pp 380-83. 888

TERRY L L: Cigarette smoking and respiratory disease. Presented at: Albert Einstein Medical Seminar. pp 1-23, 1968. 889

The Medical Journal of Australia. Oh, Mr. Snedden! 1315-6, 1971. 890

U.S. Department of Health, Education and Welfare: Cigarette smoking and health characteristics. United States -- July 1964-June 1965. National Center for Health Statistics pp 1-65, 1967. 891

VINCENT R G: A fence or an ambulance. J Sch. Health 37: 369-72, 1967. 892

U.S. Medicine: New report on smoking provides ammo for anti-tobacco forces. U.S. Med 30, 1969. 893

VOORST VADER P J A V: Bertrekkingen tussen roken en de strefte in Nederland gedurende 1963. Ned Tijdschr Geneeskd 109: 601-8, 1965. 894

WARE G W: PHS Report on smoking and cancer. Med Ann DC 33: 120, 1964. 895

WEISS W: Cigarette smoking: suicide in slow motion. Arch Environ Health 16: 1-3, 1968. 896

WYNDER E L and HOFFMANN D: Less harmful ways of smoking. J Natl Cancer Inst 48: 1749-58, 1972. 897

BIBLIOGRAPHY

VIII-C-(2). ARTICLES RELATING TO PULMONARY EMPHYSEMA

	Reprint
American Medical Association: Emphysema produced in cigaret-smoking dogs investigators report at AMA meeting. Am Med Ass 1-4, 1966.	898
American Review of Respiratory Diseases: Chronic bronchitis emphysema and related disorders. Am Rev Resp Dis 101: 794-95, 1970.	899
ANON: Breath of life. MD 206-12, 1964.	900
ANON: Cigarettes and cancer. MD 85, 1970.	901
ANON: Warning: cigarettes are dangerous to your health. 23-25, 1968.	902
Archives of Otolaryngology: Emphysema, the insidious enemy. Arch Otolaryng 90: 121, 1969.	903
AUERBACH O: Relation of smoking to lung cancer. Northwest Med 63: 240, 1964.	904
AUERBACH O, STOUT A P, HAMMOND E C and GARFINKEL L: Effect of smoking on the tracheobronchial tree and the lung parenchyma. In: University of Kentucky Tobacco and Health Workshop Proceedings, 1964, pp 18-27.	905
British Medical Journal: Enzyme deficiency and emphysema. Br Med J 3: 655-56, 1971.	906
CASSUTO J: Emphysema explained to employees. J Occup Med 12: 272-73, 1970.	907
COOKE A: Cigarettes -- the final indictment. Bad news for bald men. CA 14: 35-36, 1964.	908
FALK G A and BRISCOE W A: Alpha$_1$-antitrypsin deficiency in chronic obstructive pulmonary disease. Ann Intern Med 72: 427-29, 1970.	909
FALK G A and BRISCOE W A: Chronic obstructive pulmonary disease and heterozygous alpha$_1$-antitrypsin deficiency. Ann Intern Med 72: 595-96, 1970.	910
FISHER C M: The possible role of coughing in the pathogenesis of pulmonary emphysema. Can Med Ass J 91: 351-52, 1964.	911
GOLDSMITH J R: Los Angeles smog vs. health. Calif Health 10-15, 1971.	912
GROSS P: A biochemical pathogenetic aspect of emphysema. Arch Environ Health 15: 411, 1967.	913
GROSS P and deTREVILLE R T P: Letter to the Editor. Arch Environ Health 19: 612, 1969.	914

Journal of the Air Pollution Control: Institutional notes. J Air Pollut Control Assoc 16: 392, 1966. 915

Journal of the American Medical Association: Emphysema: several factors may cloud diagnosis. JAMA 193: 24, 1965. 916

Journal of the American Medical Association: Panelists discuss emphysema's etiology, detection, treatment. JAMA 197: 20-21, 1966. 917

Journal of the American Medical Association: US report of rare syndrome. JAMA 199: 35, 1967. 918

Journal of the American Medical Association: Emphysema warning indicated. JAMA 208: 2255, 65, 1969. 919

LARSON R K: Smoking and emphysema. Calif Sch Health 4-11, 1966. 920

LAURELL C B: Is emphysema in alpha$_1$-antitrypsin deficiency a result of autodigestion? Scand J Clin Lab Invest 28: 1-3, 1971. 921

Medical Tribune: Cigarette smoking is found common to six families reporting emphysema. Med Tribune 24, 1966. 922

Medical Tribune: Cancer from cigarettes. Smoking dogs get invasive type tumor. Med Tribune I, 20, 1970. 923

Medical Tribune: Smoking is held top habit factor in emphysema. Med Tribune 1963. 924

Medical Tribune: Cigarette-cancer dog tests challenged by tobacco group. Med Tribune 1970. 925

Medical Tribune: Emphysema: Only one thing sure -- ailment is on rise. Med Tribune 926

Medical Tribune: Lung emphysema: histologic trials only certain clue. Med Tribune 927

Medical World News: Alarming rise in emphysema: Challenge to physicians. Med World News 32-40, 1965. 928

Medical World News: Smoking plus air pollution multiphy emphysema rate. Med World News 8: 29, 1967. 929

Medical World News: Who are the 5% whose genes invite emphysema? Med World News 11: 15, 1970. 930

Nebraska State Medical Journal: Chronic bronchitis and emphysema. Nebr State Med J 53: 446-47, 1968. 931

OSWALD N C: BCG vaccination. Practitioner 201: 701, 1968. 932

PANZER F: Emphysema and smoking. N Engl J Med 286: 1321, 1972. 933

PAUL O: Smoking and youth. Ind Med Surg 287-88, 1968. 934

PETERS G A and PRICKMAN L E: Smoking is detrimental in asthma and emphysema. Minn Med 40: 116-20, 1957. 935

Physical Therapy: Emphysema now major killer of women. Smoking scored. Phys Ther 47: 238-39, 1967. 936

Physical Therapy: Study shows relationship of smoking and emphysema. Phys Ther 48: 166, 1968. 937

Public Health Report: Respiratory disease. Public Health Report 77: 971-74, 1962. 938

Rhode Island Medical Journal: Tobacco and pulmonary emphysema. RI Med J 49: 475, 1966. 939

ROBERTS K E: Emphysema and enterbacterial infections. Med Counterpoint 2: 47, 1970. 940

ROSENBLATT M B: Emphysema, quantophrenia, and medical history. Med Counterpoint 1: 14-20, 1969. 941

SACHS M I: Tenth conference of the International society of Geographical Pathology. Isr J Med Sci 6: 176-78, 1970. 942

Science News: Cigarette-smoking dogs get emphysema in tests. Sci News 90: 25, 1966. 943

SIEDLECKI J T: Emphysema -- prevalence and relation to TDI exposure. JAMA 212: 2271, 1970. 944

The Lancet: Cadmium. Lancet 2: 1346, 1969. 945

The Lancet: Antitrypsin deficiency in chronic obstructive lung disease. Lancet 1: 71, 1970. 946

The Medical Journal of Australia: Chronic obstructive lung diseases. Med J Aust 724, 1964. 947

Tuberculosis Association of Maryland: Chronic bronchitis and emphysema. Md State Med J 17: 107-8, 1968. 948

WENDOHL F F and FACKLER W A: The life cycle of Olin Ansink. Bull Natl Tuberc Resp Dis Ass 54: 3-6, 1968. 949

BIBLIOGRAPHY

VIII-C-(3). ARTICLES RELATING CHRONIC BRONCHITIS

	Reprint
British Medical Journal: Beginnings of bronchitis. 2: 190-91, 1970.	950
CARNOW B W: Pulmonary disease and air pollution. Chicago Med 71: 581-86, 1968.	951
DOLL R: Investigation into cigarette smoking and atmospheric pollution in the aetiology of lung cancer. Methods Inf Med 2: 13-19, 1963.	952
ESPINO V J: Tabaquismo y corazon. Arch Inst Cardiol Mex 37: 539-40, 1967.	953
GOLDSMITH J R: Air pollution medical research. Science 154: 1588-91, 1966.	954
GOLDSMITH J R: Synthesis, perspective, and future applications. Arch Environ Health 18: 710-14, 1969.	955
GREGG I: Chronic bronchitis and occupation. Br Med J 1: 675-76, 1966.	956
Journal of the American Medical Association: A causal role for bronchitis? 193: 26-27, 1965.	957
La Presse Medicale: Pollution atmospherique, tabac et bronchite chronique. 78: 1072, 1970.	958
Medical Times: Human costs of polluted air. 98: 156-70, 1970.	959
MITCHELL R S: Describes ramifications of smoking. Mich Med 550-51, 1966.	960
OCHSNER A: The health menace of tobacco. Am Sci 59: 246-52, 1971.	961
STURGIS K R: Is surgery for lung cancer worthwhile? 130-42, 1967.	962
STURGIS K R: The physician and air pollution. Pa Med 74: 39-40, 1971.	963
TAYLOR I: The prevention of disease in middle age. Public Health 77: 231-36, 1963.	964
The Medical Officer: The "chesty" child, chronic bronchitis, and cigarettes. 161, 1969.	965
U.S. Medicine: Air pollution held major U.S. problem. 2, 17-18, 1968.	966

BIBLIOGRAPHY

VIII-C-(4). ARTICLES RELATING TO MORTALITY STATISTICS

	Reprint
American Cancer Society News Service Release: Film on "Smoking: Past and present" traces the history of smoking. 189, 1968.	967
Asian Medical Journal: Smokers' chance for lung cancer said 11 times higher. 7: 45, 1964.	968
BARCLAY R S: Worldwide chest medicine. Chest medicine and cardiovascular conditions in Great Britain. Dis Chest 49: 559-60, 1966.	969
BORGATTA E F and EVANS R R: Smoking, health, and behavior. Aldine Publishing Company: Chicago, 1968.	970
BURCH G E: Trends in the incidence of disease in the United States. World Med J 8: 439-40, 1961.	971
BURGESS A M: Mortality from diseases associated with smoking: United States 1950-1964. RI Med J 192-93.	972
Canadian Journal of Public Health: News notes: United States. 56: 453-54, 1965.	973
Canadian Medical Association Journal: The annual meeting of the Manitoba Medical Association (Canadian Medical Association Manitoba Division). 91: 1083, 1964.	974
Canadian Medical Association Journal: Intelligent debate or demented fiddling? 96: 679-80, 1967.	975
Cancer News: New ACS report traces smoking effects in women. 18	976
CECILIONI V A: Lung cancer in Hamilton. Can Family Physician 1970.	977
FONTANA R S: Smoking and health.	978
FLETCHER C M: Cigarettes and respiratory disease. NTRDA Bulletin 12-14, 1968.	979
GARFINKEL L: Several studies show higher death rates for smokers than for nonsmokers. Public Health News 211-14, 1963.	980
HAMMOND E C: Some preliminary findings on physical complaints from a prospective study of 1,064,004 men and women. Am J Public Health 54: 11-23, 1964.	981
HAMMOND E C: Competitive risks: lung cancer, emphysema and coronary heart disease. Cancer Soc News Serv 1-10, 1967.	982
HAMMOND E C: La relacion entre el habito de fumar y las tasas de mortalidad. Orientacion Med 20: 985-92, 1971.	983
HELMHOLZ H F Jr: On diagnostic errors. Ann Allergy 26: 517-18, 1968.	984
HIGGINS I T T: Smoking. In: Aging of the Lung. Edited by L Cander and J H Moyer, Grune and Stratton: New York, pp 227-38.	985

HYATT C L: Physicians and smoking. J Arkansas Med Soc 184. 986

JONGKEES L B W: Sigaretten en spinazie. Ned Tijdschr Geneeskd 109: 530, 1965. 987

Journal of the American Medical Association: Cigarette smoking may cause small hearing loss, 210: 1845, 1969. 988

KLEIN R C: A hole in the whole case. Med Counterpoint 61, 1970. 989

LANDAU E and MORTON J: An epidemiologic view of chronic pulmonary insufficiency in the United States. Am Rev Resp Dis 83: 405-7, 1961. 990

L'Union Medicale du Canada: Augmentation du nombre de cancers pulmonaires. 97: 1850, 1968. 991

McKEE K T: The occurrence and progression of pulmonary emphysema. South Med J 56: 129-32, 1963. 992

Medical Bulletin: Warning: cigarettes are dangerous to your health. 45-47, 1968. 993

Medical Bulletin on Tobacco: Heart deaths lead cigarette effects. 5: , 1967. 994

Medical Tribune: Lung cancer seen often in smokers in Czechoslovakia. 995

Medical Tribune: Firm ties denied between cancer and air pollution. 8- 996

Medical World News: Bronchitis and emphysema increase in female smokers. 35, 1967. 997

MITCHELL R S: Outlook in emphysema and chronic bronchitis. N Engl J Med 280: 445-46, 1969. 998

Public Health Service Publication No. 1103: Cigarette smoking and cancer. 1963, 1-32. 999

RAVENHOLT R T: Cigarette smoking: magnitude of the hazard. CA 187-88, 1965. 1000

RENZETTI A D Jr, McCLEMENT J H and LITT B D: Respiratory diseases. Nebr State Med J 488-89, 1966. 1001

RYDER C F: Chronic respiratory diseases -- a mushrooming challenge. JAMWA 21: 132-36, 1966. 1002

The Journal of School Health: Cigarette smoking and cancer. A new booklet by the American Cancer Society. 266-68. 1003

WADDELL J A: Bronchitis and emphysema. Br J Clin Pract 20: 477-80, 1966. 1004

BIBLIOGRAPHY

VIII-C-(5). ARTICLES RELATING TO MORBIDITY STATISTICS

	Reprint
ANDERSON K N: Doctor with one foot in space. Today's Health 32-35, 68-69, 1964.	1005
BOIN J K: Expert MD opinions vary on major health hazard facing coal miners. U.S. Med 4, 18, 1969.	1006
BOUCOT K R: Smoking as a predisposing factor in respiratory disease. Arch Environ Health 16: 459, 1968.	1007
Canadian Medical Association Journal: Smokers who cough. 89: 1099-1100, 1963.	1008
Canadian Medical Association Journal: The lung. 100: 349-51, 1969	1009
CHRISTINE B W: Effects of cigarette smoking on Connecticut residents. Conn Health Bull 85: 23-28, 1971.	1010
College Health: The association presents its views about smoking. 2-3, 1965	1011
FERRIS B G Jr, SPEIZER F E, WORCESTER J and CHEN H Y: Adult mortality in Berlin, NH, from 1961 to 1967. Arch Environ Health 23: 434-39, 1971	1012
FORD R M: Smoking, lung cancer and asthma. Br Med J 3: 372, 1971	1013
HEPPER N G G: Cigarette smoking and chronic respiratory disease. Minn Med 52: 1373-75, 1969.	1014
HORN D: Cigarette smoking in the high schools. Calif Sch Health 17-21, 1966	1015
HORTON R J M: Discussion. Epidemiologic studies of chronic respiratory diseases. Arch Environ Health 10: 344-45, 1965	1016
JOULES H:: A preventive approach to common diseases of the lung. Br Med J 2: 1259-63, 1954	1017
Journal of Iowa Medical Society: The teen-age smoker. 220, 1969	1018
Journal of the national Medical Association: Statistics on health and cigarette smoking. 356, 1967.	1019
LORENZONI L: Med Lav 58: 769-71, 1967	1020
MASON R P: Cancer and the environment. 111, 1970	1021
Medical News: Emphysema worse out of town. 1968	1022
Medical World News: Doctors push black lung fight to surface. 10: 14-16, 1969	1023
MITCHELL R S, MAISEL J C, DART G A and SILVERS G W: The accuracy of the death certificate in reporting cause of death in adults. Am Rev Resp Dis 104: 844-50, 1971.	1024

Bibliography VIII-C-(5) Reprint

MORIYAMA I M: Chronic respiratory disease mortality in the United States. Public Health Reports 78: 743-48, 1963 1025

MORIYAMA I M, DAWBER T R and KANNEL W B: Evaluation of diagnostic information supporting medical certification of deaths from cardiovascular disease. Natl Cancer Inst Monogr 19, 405-19, 1966 1026

PEMBERTON J: Occupational lung disease. Br Med J 1: 609, 1966 1027

U.S. Medicine: Genetic factors may contribute to increased coronary ills in smokers. 16, 1968 1028

Science News Letter: Coal miners' bronchitis related to cigarettes. 86: 47, 1964 1029

BIBLIOGRAPHY

VIII-C-(6). ARTICLES RELATING TO BRONCHOPULMONARY AND CARDIOPULMONARY EFFECTS OF CIGARETTE SMOKE

	Reprints
CLOUGH P W: The irritative effect of smoking on the respiratory mucous membranes. Ann Intern Med 45: 1235-41, 1956.	1030
DEVINE K D: Pathologic effects of smoking on the larynx and oral cavity. Proc Mayo Clin 35: 349-51, 1960.	1031
Diagnosis News: Pulmonary emphysema is a "vascular disease". 2: 16-17, 19	1032
GUILLERM R, BADRE R, SAINDELLE A, HEE J and FLAVIAN N: Acquisitions recentes sur la toxicologie de la fumee de tabac. Gazette Hopitaux 140: 861-62, 1968	1033
Medical Tribune: Nicotine found to intensify calcific disease in rabbits. 29, 1968	1034
NTRDA Bulletin: Blood vessel damage caused by smoking important in emphysema. 12,	1035
OLSEN A M, FONTANA R S, PEABODY H D Jr, and ORDSTRAND H S V Relationship of smoking to chronic respiratory disease. Dis Chest 54: 189-90, 1968	1036
RAMIREZ E A: Protective factors from atherosclerosis in Puerto Rican veterans? Bol Asoc Med PR 161-62, 1969	1037
RANKIN J: The effect of smoking on pulmonary function. 24-27	1038
SACHS D P and FINLEY T N: Smoking and pulmonary macrophages. N Engl J Med 286: 788-89, 1972	1039
SHUBIN H: Pulmonary emphysema and the heart. Pa Med 69: 52, 1966	1040
TAYLOR R M: Le probleme de la cigarette. Med Hyg 895: 1450-51, 1969	1041
Tobacco Reporter: Some theories about smoking. 94: 33, 1967	1042
Tobacco Reporter: Dryden gives institute's views on health issues. 54-55, 1967	1043

BIBLIOGRAPHY

VIII-C-(7). ANTISMOKING CAMPAIGN

	Reprint
American College of Chest Physicians: Statement on cigarette smoking. Dis Chest 42: 233, 1966	1044
American Journal of Public Health: Cigarette sales in health facilities. 60: 180-81, 1970.	1045
ARING C D: On smoking and the uses of adversity. Milit Med 134: 1455, 1969.	1046
AYRES S M: The physician's role in the control of smoking. Bull N Y Acad Med 44: 1546-52, 1968.	1047
BACHMAN D S: Those unfortunate people -- the smokers. J Arkansas Med Soc 66: 329-30, 1970	1048
BANYAL A L: The fateful challenge of smoking. Dis Chest 52: 562-64, 1967.	1049
BARCKLEY V: Cigarette smoking -- the lag between knowledge and practice. Nurs Outlook 29	1050
BELCHER D: Bibliography on smoking and health for teachers and students. Calif Sch Health 47-50, 1966	1051
BELLOMY M D: Physicians are doing something about the smoking problem. Cancer Cyt 5: 49-55, 19	1052
BEUMER H M: Roken en gezondheid. N.M.G.T. 16: 11-14, 1963	1053
BROWNING R H and THORP D: Cigarettes. The Ohio thoracic society report. Ohio State Med J 65: 245-47, 1969.	1054
California Governor's Advisory Committee on Cigarette Smoking and Health: Health vs. cigarette smoking. pp 1-6, 42-45, 1964	1055
California Medical Association: A study of the attitudes and opinions of physicians on smoking. 1-34, 1967	1056
Canadian Family Physician: Do you smoke? 7-8, 1968	1057
CHADWICK D R: Chronic respiratory diseases -- a time for action. Rev Allergy 22: 1108-9, 1968	1058
COOK B A: Survey on smoking. Med J Aust 363-65, 1966	1059
COOKE S C S: The Australian tobacco research foundation. Med J Aust 975, 1970	1060
CORWIN E: Is cigarette smoking on the rise? NTRDA Bull 7-8, 10-11, 1970	1061

Bibliography VIII-C-(7) Reprint

CHRETIEN J: Usage de tabac (Tobacco usage). Evol Med 15: 328-32, 1971 1062

DAVID J C: The unequal fight against the cigarette menace. J Christ Med Ass 195-6 1063

de TAKATS G: Smoking withdrawal: the physicians role. Illinois Med J 127: 141-46, 1965 1064

DIEHL H S: The physician and cigarette smoking. New Physician 231-34, 1970 1065

DIMOND J L: Chronic bronchitis. N Z Med J 75: 38, 1972 1066

ELLIOT R and TIGHE T: Breaking the cigarette habit: effects of a technique involving threatened loss of money. Psychol Record 18; 503-13, 1968 1067

FLETCHER C M, HORN D, AS B and RAMSTROM L M: The limitation of smoking. WHO Chron 25: 452-57, 1971 1068

FODOR J T, GLASS L H and WEINER J M: Smoking behavior, cognitive skills and educational emplications. J Sch Health 94-98, 1069

FOLEY W J, AMOE H E Jr, COON W W and CULVER D H: Cigarette smoking among medical students. N Engl J Med 280: 1284-85, 1969 1070

FREDRICKSON D T: How I help people stop smoking. Hosp Physician 53-56, 1968 1071

FREDRICKSON D T: Cigarette smoking: questions patients ask doctors. Chest 58: 147-51, 1970 1072

GREEN D E and HORN D: Physicians' attitudes toward their involvement in smoking problems of patients. Dis Chest 54: 180-81, 1968 1073

HAMMOND E C: Evidence on the effects of giving up cigarette smoking. Am J Public Health 55: 682-91, 1965 1074

HARVEY C: What should we do about smoking. Bull Postgrad Committee Med 128-30, 1969. 1075

Hawaii Medical Association: Position paper on smoking and health. Hawaii Med J 27: 590-91, 1968 1076

HEDRICK J L: The economic costs of cigarette smoking. HSMHA Health Rep 86: 179-82, 1971. 1077

HEPPER N G G, CARR D T, ANDERSEN H A, FONTANA R S, ROSENOW E C and HANSON C: Antismoking clinic: report of an experience and comparison with published results. Mayo Clin Proc 45: 189-96, 1970 1078

HISLOP H J: That cloud of smoke. 44: 155, 1964 1079

JAMES G: The present status and future development of community health research -- a critique from the viewpoint of community health agencies. Ann N Y Acad Sci 107: 760-770, 789-91, 798-99, 1963 1080

JARVINEN K A J: Smoking as a problem affecting health. World Med J 7: 302, 1960 1081

Bibliography VIII-C-(7) Reprint

JONES H: Smoke, choke....Teenagers fight back with smoke-out campaign. NTRDA Bull 10-12, 1970. 1082

Journal of the American Medical Association: Psychiatrists shrink from giving up cigarettes. 219: 823, 826-28, 1972. 1083

Journal of the Mississippi State Medical Association: Mississippi M. D.'s heed Dr. Ochsner. 56 1084

LONG P H: Doctor, can you stop smoking? Med Times 92: 407-8, 1964 1085

LUBAN-PLOZZA B: De quelques possibilites de deshabituer les fumeurs. Med Hyg 803: 1337-41, 1967 1086

LUDWIG A M and PYLE R L: Danger potential of commonly abused drugs. Wis Med J 68: 216-18, 1969 1087

LYNCH H T: Antismoking clinic. Med Tribune 1088

McFARLAND J W, GIMBEL H W, DONALD W A J and FOLKENBERG E J: The five-day program to help individuals stop smoking. Conn Med 28: 885-90, 1964 1089

Medical Arts and Sciences: Cigarette labeling law. 132-33, 1965 1090

Medical Tribune: Antismoking leaders hail FCC move; battle looms. 10: 1, 24 1969. 1091

Medical Tribune: Albany College faculty supports ban on radio, TV cigarette advertising. 4, 1969. 1092

Medical Tribune: Hearings opened on FTC rulings on cigarette ads. 8, 1969. 1093

Medical Tribune: California doctors tie illnesses to cigarettes. 3, 1094

MESERVE W G: Congressional action on smoking and health. 257-62 1095

MILLER R K: Summary of proceedings of house of delegates of the Oregon Medical Association. Northwest Med 385, 388-89, 391-93, 1964 1096

MOERSCH H J: Counsel for the patient who smokes. Dis Chest 54: 211-20, 1968 1097

MOORE G E and VINCENT R G: Where do we go from here in research. 1-10, 1098

MORGAN K R: Landlord, fill the flowing bowl (and while you're at it, bring me a pack of camels). Consultant 18-19, 1968 1099

MUELLER M: Anti-smoking forces gain ground. Science 165: 569, 1969 1100

MYDLIL F and TOMANEK A: Koureni cigaret a plicni choroby. Rozhledy Tuberk Nemocech Plincnich 24: 649-50, 1964 1101

Bibliography VIII-C-(7). Reprints

OCHSNER A: Formal recommendations of the national forum on office management of smoking problems. Dis Chest 54: 170-73, 1968. 1102

OCHSNER A: The time is now. Med Tribune 1, 11, 1103

OCHSNER A: The physician's responsibility in the smoking problem. Med Tribune 1104

ORR H B: Hazards and evidence. Med Tribune 10: 1969 1105

PAGE I H: Cigarettes and the ambivalent American. Modern Med 59-61, 1967 1106

PALMER D H: Inconsistent policies. Med Tribune 1107

PEABODY J W Sr: Role of cigarette smoking in the causation of disease. Med Ann DC 31: 702-3, 1962 1108

Pennsylvania Health: Sixteen stopped smoking. 26: 9-10, 1965 1109

Pennsylvania Medicine: Smoking and health week. 72: 8, 1969 1110

PETTY T L: Curbing smoking in hospitals. Am Med News 1111

PICK W: Prevention of lung cancer. N Engl J Med 262: 1244-45, 1960 1112

PLATT D and BOINES G J: Physicians and smoking. Del Med J 70, 72, 1965 1113

Public Health Reports: Smoking and health. 82: 231-32, 1967 1114

PUTZ C: La nocivite des poussieres de scorie Thomas sur l'arbre respiratoire et la prevention des broncho-pneumopathies. Arch Mal Prof 30: 147-50, 1969 1115

RADELFINGER S: Opinion. Calif Sch Health 44 1116

RONKA E K F: Smoking and emphysema. N Engl J Med 263: 979, 1960 1117

ROSENBERG A: An attempt to break the smoking habit. Appl Ther 4: 1029-33, 1962 1118

RYAN W J: Mind if I smoke, doctor? The Bulletin 1968 1119

Science News: New smoking tactics. 91: 447-48, 1967 1120

SEPPILLI A: Fumo di sigarette grave problema di sanita pubblica: Minerva Med 1121

SIDEL N: The periodic health examination: how worthwhile? Consultant 7: 10-12, 1967 1122

SIRTORI C: Analisi scientifica e sociale del fumo. Minerva Med 299-300 1123

SPIEGEL H and COHEN S B: Clinical confrontation: is hypnosis an effective deterrent to smoking. Med Opinion Rev 66-67, 71, 75, 1970 1124

Bibliography VIII-C-(7). Reprints

STEWART W H: Influencing smoking behavior. Presented at World Conference on Smoking and Health. 1967, 1-10 1125

STREIT W K: Smoke now -- pay later. 1126

STUBER R V: Smoking -- where do we stand? Mich Med 324, 329, 1967 1127

TERRIS M: A social policy for health. Am J Public Health 58: 5-12, 1968 1128

TERRY L: Smoking habits -- trends and advances. 3-5, 8-9, 1129

The Chart: Cigarettes to go. 1130

The Journal of School Health: Smoking and health. 403-4 1131

The Lancet: Does it help to stop smoking. 1: 238-39, 1972 1132

The Medical Journal of Australia: To smoke or not to smoke. 346-47, 1970 1133

U.S. Medicine: Strong health warning in cigarette ads urged. 18, 1960 1134

WARING G: Report from Ottawa. Can Med Ass J 100: 1063, 1969. 1135

Weschester Medical Bulletin: Smokers' withdrawal clinic. 17-18, 1969 1136

World Health Organization: Health consequences of smoking. In: Twenty-third World Health Assembly, 1970. 15-16 1137

ZAGONA S V: Studies and issues in smoking behavior. The University of Arizona Press: Tucson, 1967. 1-256 1138

BIBLIOGRAPHY

VIII-C-(8). ARGUMENTS AGAINST SURGEON GENERAL'S STATEMENT

	Reprint
American Druggist: In Defense of cigarettes. 83-84, 89, 1970	1139
BARACH A L: Storage of pleasures: the physician's role. Geriatrics 22: 73-74, 1967	1140
BARACH A L: Tobacco smoking and the humanities. JAMA 212: 1525, 1970	1141
BELL J A E: Mortality rates of smokers.	1142
BROWNLEE K A: A review of "smoking and health" 722-39	1143
CHADWICK D R: Chronic respiratory diseases -- something can be done. NTA Bull 9-11, 1967.	1144
DELARUE N C: Cigarette smoking: A clinical and public health challenge. Can Med Ass J 87: 961-69, 1962.	1145
HAHN M J Jr, WESTINGHOUSE W D, SCHREIBER S J, BRILLMAN C R, LOMBARD R T and EISENBERG M: Should a strong attempt be made to get old people to change habits like smoking and overeating. Geriatrics 25: 68, 71, 1970	1146
HUKILL P B: Opening wedge. N Engl J Med 269: 988, 1963	1147
KOTIN P: University of Kentucky tobacco and health workshop proceedings. 1967 28-38	1148
KOTIN P: The cigarette -- lung cancer imbroglio and public opinion. JAMA 211: 506, 1970	1149
LEVIN M L: Recent epidemiological research in the relationship between cigarette consumption and health at Roswell Park Memorial Institute. 1-9	1150
MALLAN L: It is safe to smoke. Hawthorn Books Inc: New York City 9-23	1151
MATOUSEK W: Smoking: a basis for advice to the patient. Am Practitioner 8: 1226-28, 1957	1152
New England Medical Journal: Bulletin on tobacco. 268: 1087, 1963	1153
OVERHOLT R H: The physician's obligation in the smoking issue. NY State J Med 64: 1297-1300, 1964.	1154
ROLLINS I M: Two viewpoints -- a factual presentation of the smoking controversy. In: Charlotte Postgraduate Seminar, 1969. 1-15	1155

Bibliography VIII-C-(8) Reprint

SCHUMANN L M: Approaches to primary prevention of disease. Public Health Reports 85: 1-10, 1970. 1156

SIMON J L: A reply to Brownlee on "Smoking and health". Am Stat 35-36, 1966 1157

STEINFELD J L: The physician's role: the physician's responsibility to his smoking patients. RI Med J 119-123, 1972 1158

WARTHEN H J: The tobacco Report. Va Med J 91: 130-31, 1964 1159

IX. RECOMMENDATIONS

The reviewer is submitting the following recommendations to the Council for Tobacco Research:

1. Publication. That cigarette smoking is one of several risk factors and not the most important cause of chronic pulmonary disease should be publicized to the medical profession and the general public. Portions of this review can be expanded and modified for publication and distribution.

2. Epidemiology. The expert advice of a statistician is needed to review mortality statistics, specifically to analyze the death rate for pulmonary emphysema separately from that for chronic bronchitis. The morbidity statistics should also be examined for regional differences in the United States and comparison between countries.

3. Clinical investigation. A five-year follow-up of smokers should be conducted to determine whether those with early signs of ventilatory function develop pulmonary emphysema or chronic bronchitis.

4. Pathological investigation. A registry of persons who have been smokers for 50 years would be helpful in determining the influence of cigarette smoking.

5. Animal investigation. Attempts to induce pulmonary emphysema or chronic bronchitis in animals should continue. The emphasis should be given to determining the relative importance of air pollution, infection and cigarette smoking in the same laboratory model.

X. ADDITIONAL BIBLIOGRAPHIC LISTS

Additional Bibliographic List No. 1

PULMONARY EMPHYSEMA: ETIOLOGY AND PATHOGENESIS

	Reprint
ADELMAN J U: A review and reappraisal of emphysema. Dis Chest 51: 156-61, 1967.	A 1
BISHOP W R: Pulmonary emphysema. Proc Med Sec Amer Life Convention 51st annual meeting-June 24-26, p. 118-22, 1963.	A 2
EBERT R V, and PIERCE J A: Pathogenesis of pulmonary emphysema. Arch Intern Med 111:34-43, 1963.	A 3
GOUGH J. The pathogenesis of emphysema. In: The Lung, edited by Averill A. Liebow and David E. Smith, The Williams and Wilkins Co., Baltimore, 109-33, 1968.	A 4
ISHIKAWA S, FATTAL G A, ZYLAK C, CHERNIACK R M and WYATT J P: A postmortem study of viscoelastic properities of lung in emphysema (correlation with quantitative morphometry). Pub Hlth Serv No 1787: 325-37, 1968.	A 5
KLEIN R C: The etiology of emphysema. Med Counterpoint 2: 13-17, 1970.	A 6
MITCHELL R S, TOLL G and FILLEY G F: The early lesions in pulmonary emphysema. Amer J Med Sci 243: 409-18, 1962.	A 7
RODMAN T and STERLING F H: Etiology and pathogenesis. In: Pulmonary Emphysema and Related Lung Diseases, The C. V. Mosby Co., St. Louis, 3-23, 1969.	A 8
THOMPSON W T: What is emphysema? Virginia Med Month 97: 65-7, 1970.	A 9
TOMASHEFSKI J F and PRATT P C: Pulmonary emphysema: pathology and pathogenesis. Med Clin N Amer 51: 269-81, 1967.	A 10
WRIGHT G W and KLEINERMAN J: A consideration of the etiology of emphysema in terms of contemporary knowledge. Amer Rev Resp Dis 88: 605-20, 1963.	A 11

Additional Bibliographic List No. 2

PULMONARY EMPHYSEMA: PATHOLOGICAL FEATURES

	Reprint
ANDERSON A E, Jr. and FORAKER A G : Populations of nonrespiratory bronchioles in pulmonary emphysema. Arch Pathol 83: 286-92, 1967.	A 12
ANDERSON W F, ANDERSON A E, Jr., HERNANDEZ J A and FORAKER A G: Topography of aging and emphysematous lungs. Amer Rev Resp Dis 90: 411-23, 1964.	A 13
BRUN J, FOFMAN J, GUICHARD A AND PERRIN-FAYOLLE M: L'emphysème bilieux disséminé a évolution progressivement destructive. Poumon Coeur 23: 1049-70, 1967.	A 14
CAMPBELL P E: Congenital lobar emphysema. Aust Paediatric J 5: 226-233, 1969.	A 15
CROXATTO O C and OLMEDO G: Relacion entre el "Enfisema Apical O Marginal Minimo" con el enfisema extendid bilateral. Medicina 28: 281-5, 1968.	A 16
GOUGH J: The pathology of emphysema. Postgrad Med J 41: 392-400, 1955.	A 17
GROSS P: Pathological anatomy of emphysema associated with known occupational diseases. In: Emphysema in Industry, Medical Series Bulletin No. 10, Pittsburgh, p. 90-98, 1966.	A 18
HERNANDEZ J A, ANDERSON A E, Jr., HOLMES W L AND FORAKER A G: Macroscopic relations in emphysematous and aging lungs. Geriatrics 21: 155-66, 1966.	A 19
JERRY L M AND RITCHIE M B: Bronchiolar emphysema. Canad Med Ass J 90: 964-9, 1964.	A 20
MITCHELL R S, WALKER S H, SILVERS G W, DART G and MAISEL J C: Frequency and severity of anatomic emphysema in men over 40 dying in two Denver hospitals. Arch Environ Hlth 18: 667-70, 1969.	A 21
NEWMAN J K, VATTER A E and REISS O K: Chemical and electron microscopic studies of the black pigment of the human lung. Arch Environ Hlth 15: 420-9, 1967.	A 22
OTTO V H: Das unspezifische respiratorische syndrom. Fortschr Med 87: 1394-8, 1969.	A 23
PRATT P C: Intrapulmonary radial traction: measurement, magnitude and mechanics. Pub Hlth Serv Pub no. 1879: 159-181, 1969.	A 24
PRATT P C and KILBURN D H: Modern concept of the emphysemas based on correlations of structure and function. Hum Path 1: 443-63, 1970.	A 25
PRATT P C, JUTABHA P and KLUGH G A: The relationship between pigment deposits and lesions in normal and centrilobular emphysematous lungs. Amer Rev Resp Dis 87: 245-56, 1963.	A 26
RIVERO S. O: Enfisema pulmonar. Gac Med Mex 96: 751-5, 1966.	A 27

List No. 2

Reprint

RYDER R C, THURLBECK M and GOUGH J: A study of interobserver variation in the assessment of the amount of pulmonary emphysema in paper-mounted whole lung sections. Amer Rev Resp Dis 99: 354-64, 1969. A 28

SADOUL P: Conceptions actuelles sur l'emphysème pulmonaire. Vie Med 49: 909-34, 1968. A 29

THURLBECK WM: The anatomy and histology of chronic bronchitis and all forms of emphysema. In: Emphysema in Industry, Medical Series Bulletin No. 10, Pittsburgh, p. 1-20, 1966. A 30

THURLBECK W M: A pathologist looks at respiratory failure due to obstructive lung disease. Chest 58 (4 Suppl. 2): 408-14, 1970. A 31

THURLBECK W M: Present concepts of the pathology and pathogenesis of pulmonary emphysema. Path Microbiol 35: 130-33, 1970. A 32

WORTH, G, MUYSERS K and SMIDT U: Das Lungenemphysem. Fortschr Med 86: 361-64, 1968. A 33

WRIGHT RR: Chronic pulmonary emphysema. Arch. Path. 85: 231-6, 1968. A 34

WYATT J P and FISCHER V: Emphysema and ... Industr Med Surg 33: 213-19, 1964. A 35

Additional Bibliographic List No. 3

PULMONARY EMPHYSEMA: CLINICAL FEATURES

	Reprint
BANYAI A L: Pulmonary emphysema. Geratrics 17: 548-59, 1962.	A 36
BANYAI A L: Pneumoclasia. Denominador común del enfisema pulmonar. Presna Med Argentina 53: 110-13, 1966.	A 37
BATES D V: The challenge of pulmonary emphysema. Med Coll Va Quart 1: 34-41, 1965.	A 38
BATES D V: The diagnosis of emphysema. Pathol Microbiol 35: 134-37, 1970.	A 39
BAUMANN H R: Zur behandlung des Lungenemphysems. Therap Umschau 25: 592-98, 1968.	A 40
BURROWS B: Emphysema. Presented at Chicago Medical Society Clinical Conference February 28, 1968.	A 41
CARIELLO M: Interesse medico-social dell'indagine spirografica di routine.	A 42
COLP C, PARK S S and WILLIAMS M H, Jr: Emphysema with little airway obstruction. Amer Rev Resp Dis 101: 615-19, 1970.	A 43
EBERT R V: Summary of the conference. Amer Rev Resp Dis 80: 209-12, 1959.	A 44
FEGIZ G: Problemi clinico-pathogenetici e sociali dell'enfisema polmonare. 976-92,	A 45
FLETCHER C M: Summary of conference. Amer Rev Resp Dis 95: 895-99, 1967.	A 46
GARDINER J F: Chronic obstructive emphysema. J Omaha Clin Soc 23: 133-36, 1968.	A 47
GLUCKMAN J C: L'emphysème pulmonaire. Gaz Hop 141:341-43, 1969.	A 48
HYDE L and HYDE B: Chronic pulmonary emphysema. Postgrad Med 20: 609-14, 1956.	A 49
JOHNSTON R F and KAUFFMAN L A: Pulmonary emphysema. Current Therap 1970: 104-6, 1970.	A 50
JULICH H and RUCKER K: Der einfluss von pulmophyllin auf die körperliche leistungsfähigkeit von kranken mit lungenemphysem. Dtsch Gesund 24: 346-49, 1969.	A 51
LECKERT J T: Modern trends in the diagnosis and therapy of pulmonary emphysema. J Louisiana Med Soc 116: 318-28, 1964.	A 52
LAWS J W and HEARD B E: Emphysema and the chest film: a retrospective radiological and pathological study. Bull J Radiol 35: 750-61, 1962.	A 53
LYONS H A: Obstructive pulmonary emphysema. Med Times 93: 1386-1401, 1965.	A 54
MACKLEM P: Summary of the 13th Aspen emphysema conference. Chest 59: (Supplement 5) 40S-43S, 1971.	A 55

List No. 3

McCOY W T and ROBBINS L L: Emphysema: The pulmonary enigma. Texas J Med 49: 15-18, 1963. A 56

MOTLEY H L: Pulmonary emphysema. Missouri Med 57: 701-9, 1960. A 57

NICKLAUS T M, STOWELL D W, CHRISTIANSEN W R and RENZETTI A D, Jr.: The accuracy of the roentgenologic diagnosis of chronic pulmonary emphysema. Amer Rev Resp Dis 93: 889-99, 1966. A 58

REBORA F: Formas clinicas. Gaceta Med Mexico 756-76, 1965. A 59

REID, L and MILLARD F J C: Correlation between radiological diagnosis and structural lung changes in emphysema. Clin Radiol 15: 307-11, 1964. A 60

ROKSETH R, SCHAANNING J and AAS T W: Cardiopulmonary function tests in fibrosis and emphysema. Acta Tuber Scand 46: 57-64, 1965. A 61

SADOUL P, LAXENAIRE M C, LAMBERT H and BERNADAC P: Tableau fonctionnel de l'emphyseme radiologiquement destructif. J Francais Med Chirc Thorax 24: 183-204, 1970. A 62

SCADDING J G: Emphysema. Proc Roy Soc Med 62: 1023-24, 1969. A 63

SIMON G: Radiology and emphysema. Clin Radiol 15: 293-306, 1964. A 64

SIMPSON T: The emphysema problem. Brit J Dis Chest 62: 188-94, 1968. A 65

SUTINEN S, CHRISTOFORIDIS A J, KLUGH G A and PRATT P C: Roentgenologic criteria for the recognition of nonsymptomatic pulmonary emphysema. Amer Rev Resp Dis 91: 69-76, 1965. A 66

SWINNY B, SWINNY B, Jr. and HICKS R R: Pulmonary emphysema. Southern Med J 58: 600-5, 1965. A 67

THURLBECK W M, BATES D V, FRASER R G and HENDERSON J: Morphologic and functional studies in emphysema. In: Form and Function in the Human Lung, Edited by G. Cumming and L B Hunt, E and S Livingstone LTD, Edinburgh and London, 225-48, 1968. A 68

TOLL G D: Pulmonary emphysema. Rocky Mountain Med J. 25-27, 1964. A 69

WRIGHT G W: Summary of the conference. Med Thorac 22: 420-31, 1965. A 70

Additional Bibliographic List No. 4

PULMONARY EMPHYSEMA: THERAPY

	Reprint
BADGER T L and GREEN G M: Advances in the treatment of respiratory disorders. Practitioner 199: 455-64, 1967.	A 71
BAKER L M: The use and results of diagnostic and therapeutic bronchoscopies in a prison population. J Amer Osteopath Ass 69: 646-52, 1970.	A 72
BANYAI A L: Pathogenesis and treatment of pulmonary emphysema. J Med Ass Georgia 50: 469-75, 1961.	A 73
BARACH A L: Respiración diafragmática y ejercicio con suministro concomitante de oxígeno en el tratamiento del enfisema pulmonar. Prensa Méd Argent 53: 114-9, 1966.	A 74
BASS H, WHITCOMB J F and FORMAN R: Exercise training: therapy for patients with chronic obstructive pulmonary disease. Chest 57: 116-21, 1970.	A 75
BEDELL G N and SEEBOHM P M: Treatment of pulmonary emphysema. JAMA 169: 1699-1702, 1959.	A 76
BLAKE J M: Management of pulmonary insufficiency. N Y State J Med 64: 1308-12, 1964.	A 77
BOREN H G, BUSET J F, CORPE R F, GRZYBOWSKI S, NEWMAN M M, ORGANICK, A B and LESTER W: Treatment of drug-resistant tuberculosis. Amer Rev Resp Dis 94: 125-7, 1966.	A 78
CARABASI R J: Chronic ventilatory insufficiency and its management. Clin Med 70: 725-37, 1963.	A 79
COLE M B and HAMMEL J V: Management of the emphysematous patient. Med Times 89: 1026-30, 1961.	A 80
CORAZZA L J, MORROW C S and CHESNEY T A: Triamcinolone in the therapy of chronic bronchitis and pulmonary emphysema. Amer J Med Sci 242: 436-42, 1961.	A 81
CORPE R F, GRZYBOWSKI S, MACDONALD F M, NEWMAN M M, NIDEN A H, ORGANICK A B and LESTER W: Chronic obstructive lung disease. Amer Rev Resp Dis 92: 513-8, 1965.	A 82
CURTIS J K, LISKA A P, RASMUSSEN H K and CREE E M: IPPB therapy in chronic obstructive pulmonary disease. JAMA 206: 1037-40, 1968.	A 83
DEANE R S: Aspects of respiratory therapy. Med Proceedings 14: 51-6, 1968.	A 84
DELARUE N C, WOOLF C B and STRASBERG S M: The surgical treatment of pulmonary emphysema. Canad Med Assoc J 93: 629-38, 1965.	A 85

List No. 4 Reprint

EMIRGIL C, SOBOL B J, NORMAN J, MOSKOWITZ E, GOYAL P and WADHWANI B: A study of the long-term effect of therapy in chronic obstructive pulmonary disease. Amer J Med 47: 367-77, 1969. A 86

FAIN W R: Surgery in pulmonary emphysema. Southern Med J 64: 65-75, 1971. A 87

FRANKLIN W, MICHELSON A L, LOWELL F C and SCHILLER L W: Bronchodilators and corticosteroids in the treatment of obstructive pulmonary emphysema. New Engl J Med 258: 774-8, 1958. A 88

HEAD J M, HEAD L R, HUDSON T R and HEAD J R: The surgical treatment of emphysematous blebs and localized vesicular and bullous emphysema. J Thorac Cardiovasc Surg 40: 443-60, 1960. A 89

HEPPER N G G and HYATT R E: Office management of chronic bronchitis and emphysema. Med Clin N Amer 48: 857-65, 1964. A 90

HEPPER N G, BRANSCOMB B V, CHERNIACK R, PIERCE A K and MITCHELL R S: Home and clinic care of patients with chronic obstructive lung disease. Aspen Emphysema Conf 8: 28-34, 1965. A 91

JACKSON D and BERNARD L A: Treatment for bullous emphysema. Med Record Annals 61: 113-6, 1968. A 92

JOANNIDES M, Jr.: Chronic obstructive emphysema. The thoracic surgeon's position. JAMA 192: 365-7, 1965. A 93

JOHNSTON R F and HARRIS H W: Management of chronic bronchitis and pulmonary emphysema. Med Clin N Amer 49: 1309-24, 1965. A 94

JONES N L, JONES G and EDWARDS R H T: Exercise tolerance in chronic airway obstruction. Am Rev Resp Dis 103: 477-94, 1971. A 95

KILBURN K H: Pathogenesis and treatment of chronic bronchitis. Med Times 95: 161-76 1967. A 96

KILPATRICK G S: Advances in the treatment of respiratory disorders. Practitioner 207: 460-7, 1971. A 97

KIRSCHENFELD J J: Office evaluation and management of the patient with chronic pulmonary disease. Southern Med J 56: 193-205, 1963. A 98

LEBOVITZ J J, LEBOVITZ E and SILVERMAN J D: Pulmonary emphysema. Current Therap 113-6, 1969. A 99

LEVINE B E, BIGELOW D B, HAMSTRA R D, BECKWITT H J, MITCHELL R S, NETT L M, STEPHEN T A and PETTY T L: The role of long-term continuous oxygen administration in patients with chronic airway obstruction with hypoxemia. Ann Intern Med 66: 639-59, 1967. A 100

LOPEZ-MAJANO V, KIEFFER R F, MARINE D N, GARCIA D A and WAGNER H N, Jr.: Pulmonary resection in bullous disease. Amer Rev Resp Dis 99: 554-64, 1969. A 101

List No. 4

	Reprint
MAYOCK R L: Obstructive pulmonary emphysema. G P 16: 109-20, 1957.	A 102
MILLER W F: Rehabilitation of patients with chronic obstructive lung disease. Med Clin N Amer 51: 349-61, 1967.	A 103
MITTMAN C: The management of chronic obstructive lung disease. Chicago Med 70: 177-81, 1967.	A 104
OSWALD N: Antibiotics and chronic bronchitis. Practitioner 193: 735-9, 1964.	A 105
OSWALD N: Modern day treatment of chronic bronchitis. Geriatrics 22: 125-32, 1967.	A 106
PASQUAZZI M: La terapia dell'angina pectoris. Policlinico 75: 313-25, 1968.	A 107
PETTY T L: Can anything be done for emphysema? J Louisiana State M Soc 122: 216-8, 1970.	A 108
PETTY T L and NETT L M: Patient education and emphysema care. Med Times 97: 117-30, 1969.	A 109
REEVES J E: Pulmonary emphysema in general practice. Med Times 90: 512-7, , 1962.	A 110
RICCITELLI M L: Modern concepts in the management of emphysema in the aged and infirm. J Amer Geriatrics Soc 14: 497-504, 1966.	A 111
SCADDING J G: Treatment of chronic bronchitis. Brit Med J 1: 1281-3, 1966.	A 112
SCHWABER J R: The years beyond smoking. Geriatrics 23: 106-12 , 1968.	A 113
SNIDER, G L: Ambulatory management of chronic obstructive lung disease. Wisconsin Med J 67: 229-32, 1968.	A 114
SPEAR H C, DAUGHTRY DC, CHESNEY J G and MARKS A: The surgical management of large pulmonary blebs and bullae. Amer. Rev. Resp Dis 84: 186-96, 1961.	A 115
STORY SH, Jr.: The management of pulmonary emphysema. J Med Assoc Georgia 53: 24-5 1964.	A 116
SZUCS M M, Jr. and LORD G P: Outpatient treatment of chronic obstructive pulmonary disease (COPD). J Maine Med Assoc 58: 209-10, 1967.	A 117
ULMER W T: Chronic obstructive airway disease. Recent aspects of diagnosis and treatment. S Afr Med J 46: 146-51, 1972.	A 118
WATERMAN DH, DOMM S E, ROGERS WK and BORRELL J L: The effective use of bronchoscopy in chronic bronchitis. Ann Otol Rhinol Laryngol 78: 449-58, 1969.	A 119
YANDA R L: Hyperbaric research in chronic pulmonary disease. Amer Rev Resp Dis 92: 564-78, 1965.	A 120
YANDA R L and MOTLEY H L: Changes in lung volume and spirometric measurements in emphysema patients who have been exposed to hyperbaric pressure levels. Dis Chest 47: 360-66, 1965.	A 121

Additional Bibliographic List No. 5

PULMONARY EMPHYSEMA: ALPHA$_1$-ANTITRYPSIN DEFICIENCY

	Reprint
ABLIN R: Association of alpha$_1$-antitrypsin deficiency and primary pulmonary emphysema as determined by the method of radial immunodiffusion. Acta Biol Med Germ 27: 667-670. 1971.	A 122
BRUN J, BIOT N and KOFMAN J: Hypoglobulinémie avec déficit en alpha-antitrypsine au cours d'une nouvelle observation d'emphysème familial destructif. Marseille Med. 106: 918-922, 1969.	A 123
FALK G A, SISKIND G W and SMITH, J P, Jr: Chronic obstructive pulmonary disease: a subgroup of patients identified by serum alpha$_1$-antitrypsin and immunoglobulin concentrations. Amer Rev Resp Dis 103: 18-25, 1971.	A 124
GLAUSER M-P: Le déficit en α_1-antitrypsine, associé a l'emphysème pulmonaire. Schweigerisch Med Wschr 101: 949-954, 1971.	A 125
GUENTER C A, WELCH M H, FERGUSON S, HENDERSON L and HAMMARSTEN J F: Alpha$_1$-antitrypsin deficiency: heterozygosity, intermediate levels, and pulmonary disease. Chest 59:(suppl 5) 16S-17S, 1971.	A 126
GUENTER CA, WELCH MH, RUSSEL TR, HYDE RM and HAMMARSTEN JF: The pattern of lung disease associated with alpha$_1$ antitrypsin deficiency. Arch Intern Med 122: 254-57, 1968.	A 127
HAMMARSTEN JF, WELCH MH, RICHARDSON RH, PATTERSON CD and GUENTER CA: Familial alpha$_1$-antitrypsin deficiency and pulmonary emphysema. Trans Amer Clin Climatological Ass 80: 7-14, 1968.	A 128
HOLE BV and WASSERMAN K: Familial emphysema. Ann Intern Med 63: 1009-10017, 1965.	A 129
HURST A: Familial emphysema. Amer Rev Resp Dis 80: 179-80, 1959.	A 130
KOWALYSHYN T and SATALINE LR: Familial emphysema associated with antitrypsin deficiency. Dis Chest 55: 293-9, 1969.	A 131
KUEPPERS F: Identification of the heterozygous state for the α_1-antitrypsin deficiency gene in man. Biochem Genetics 3: 283-88, 1969.	A 132
KUEPPERS F: Alpha$_1$-antitrypsin: 1. Evidence for two genes causing low concentrations in serum: 2. Association of heterozygosity and chronic obstructive lung disease. Chest 59: (Suppl 5) 15S-16S, 1971.	A 133
KUEPPERS F: Alpha$_1$-antitrypsin: physiology, genetics and pathology. Humangenetik 11: 177-89, 1971.	A 134
KUEPPERS F, FALLAT, R and LARSON RK: Obstructive lung disease and α_1-antitrypsin deficiency gene heterozgosity. Science 165: 899-901, 1969.	A 135
LARSON RK and BARMAN ML: The familial occurrence of chronic obstructive pulmonary disease. Ann Intern Med 63: 1001-8, 1965.	A 136
LEBRUN-BRAIS L, BLANCHETTE G and PROVOST G: Emphysème pulmonaire par déficience en alpha$_1$-antitrypsine: une étude familiale. Union Med Canad 100: 1920-34, 1971.	A 137

LIEBERMAN J: Heterozygous and homozygous alpha$_1$-antitrypsin deficiency in patients with pulmonary emphysema. New Engl J Med 281: 279-84, 1969. A 138

LIEBERMAN J, MITTMAN C and SCHNEIDER AS: Screening for homozygous and heterozygous α_1-antitrypsin deficiency. JAMA 210: 2055-60, 1969. A 139

MILLER F and KUSCHNER M: Alpha$_1$-antitrypsin deficiency, emphysema, necrotizing angiitis and glomerulonephritis. Amer J Med 46: 615-23, 1969. A 140

MITTMAN C: Summary of symposium on pulmonary emphysema and proteolysis. Amer Rev Resp Dis 105: 430-48, 1972. A 141

NOMIYAMA K, NOMIYAMA H and MATSUI H: Prevalence of α_1-antitrypsin deficiency in Japan. Bull WHO 45: 253-55, 1971. A 142

RESNICK H, LAPP, NL and MORGAN WKC: Serum trypsin inhibitor concentrations in coal miners with respiratory symptoms. JAMA 215: 1101-5, 1971. A 143

SANO T, YOKOYAMA M and RHOADS GG: Clinical significance of α_1-antitrypsin level. A preliminary evaluation among Japanese men Hawaii Med J 31: 27-32, 1972. A 144

SCHLEUSENER A, TALAMO RC, PARE JAP and THURLBECK WM: Familial emphysema. Amer Rev Resp Dis 98: 692-6, 1968. A 145

SMITH JP, FALK GA and SISKIND GW: Serum immunoglobulins and alpha$_1$-antitrypsin: Variation with clinical type of chronic obstructive pulmonary disease. Chest 59 (Suppl 5) 17S-19S, 1971. A 146

STEVEN P M, Hnilica V, Johnson P C and BELL RC: Pathophysiology of hereditary emphysema. Chest 59: (Suppl) 19S, 1971. A 147

SZCZEKLIK A, TERESIAK T and KOLACZKOWSKA B: Zachowanie sie antytrypsyny alfa$_1$ w surowicy krwi u ludzi zdrowych i chorych na rozedme pluc. Pol Tyg Lekar 26: 1569-71, 1971 A 148

TALAMO RC: The α_1-antitrypsin in man. J Allerg Clin Immunol 48: 240-50, 1971. A 149

TALAMO R C, AUSTEN K F and ALLEN J D: Familial emphysema and alpha$_1$-antitrypsin deficiency. Public Hlth Service No. 1787 491-95, 1972. A 150

TALAMO RC, BLENNERHASSET JB and AUSTEN K F: Familial emphysema and alpha$_1$-antitrypsin deficiency. New Engl J Med 275: 1301-5, 1966. A 151

TARKOFF M P, KUEPPERS F and Miller W F: Pulmonary emphysema and alpha$_1$-antitrypsin deficiency. Amer J Med 45: 220-28, 1968. A 152

TOWNLEY R G, RYNING F, LYNCH H and BRODY A W: Obstructive lung disease in hereditary α_1-antitrypsin deficiency. JAMA 214: 325-31, 1970. A 153

TURINO GM: Proteolytic mechanisms and pulmonary emphysema. Bull Physiol Pathol Resp 7: 719-27, 1971. A 154

VARPELA E and SARIS NE: Hereditary alpha$_1$-antitrypsin deficiency. Ann Clin Res 3: 46-53, 1971. A 155

VIDAL J, CAZAL P, ROBINET-LEVY M and MICHEL F B: Bronchopneumopathies chroniques familiales et déficit homozygote en α-1 antitrypsine. Poumon Coeui 27: 79-94, 1971. A 156

WELCH M H, REINECKE M E, HAMMARSTEN JF and GUENTER C A: Antitrypsin deficiency in pulmonary disease: the significance of intermediate levels. Ann Intern Med 71: 533-42, 1969. A 157

Additional Bibliographic List No. 6

CHRONIC BRONCHITIS

Reprint

ASHLEY D J B: Environmental factors in the aetiology of lung cancer and bronchitis. Brit J Prev Soc Med 23: 258-62, 1969. A 158

EDWARDS G: Acute bronchitis -- aetiology, diagnosis, and management. Brit Med J 1: 963-66, April 16, 1966. A 159

FLETCHER C M: Chronic bronchitis. Its prevalence, nature, and pathogenesis. Amer Rev Resp Dis 80: 483-94, 1959. A 160

FLETCHER C M: Définition, classification et étiologie de la bronchite chronique. Le Poumon Le Coeur 21: 1239-48, 1965. A 161

FLETCHER C M: Some recent advances in the prevention and treatment of chronic bronchitis and related disorders. With special reference to the effects of cigarette smoking. Proc Roy Soc Med 58: 918-28, 1965. A 162

FLETCHER C M: Recent clinical and epidemiological studies of chronic bronchitis. Scand J Resp Dis 48: 285-93, 1967. A 163

FLETCHER C M: Bronchial infection and reactivity in chronic bronchitis. J Roy Coll Phys Lond 2: 183-90, 1968. A 164

GEISLER L: Zum problem der chronisch-obstruktiven bronchitis. Deutsches Medizinisches Journal 17: 184-7, 1966. A 165

HAIN E: Soziale Bedeutung und Gestaltungsfaktoren des, Bronchitischen Syndroms. Internist 10: 144-54, 1969. A 166

HARTUNG W and MEYER-CARLSTADT D: Reid's index in the diagnosis of chronic bronchitis. Beitraege zur Pathologischen Anatomie und Allgemeinen Pathologie 137: 85-98, 1968. A 167

KAATZSCH H: Der Einflub des Rauchens auf die Ventilationsstörung des Bronchitikers. Med Klin 64: 2196-9, 1969. A 168

LICKINT F: Neuere Erkenntnisse auf dem Gebiete der Beziehungen zwischen Raucherbronchitis und Bronchialkrebs. Verh Deut Ges Inn Med 62: 121-25, 1956. A 169

LOOSLI C G: Synergism between respiratory viruses and bacteria. Yale J Biol Med 40(5-6): 522-40, 1968. A 170

LOWE C R: Chronic bronchitis and occupation. Proc Roy Soc Med. 61: 98-102, 1968. A 171

MACKLEM P T: Airway obstruction and collateral ventilation. Physiological Rev 51(2): 368-436, April 1971. A 172

MICZOCH F: Zivilisationsschäden in der Entstehung und Behandlung der chronischen Bronchitis. Wiener Klinische Wschr 77: 506-8, 1965. A 173

MORGAN W K C: Chronic bronchitis. The "English disease." Postgrad Med 41: 190-94, 1967. A 174

NEGREIROS B: Aspectos Anatomofisiopatologicos. Rev Brasileira Med 25: 457-61, 1968. A 175

PEMBERTON J: Occupational factors in chronic bronchitis. Proc Roy Soc Med 61: 95-98, 1968. A 176

PHILLIPS A M, PHILLIPS R W and THOMPSON J L: Chronic cough: analysis of etiologic

REID L: Chronic bronchitis and hypersecretion of mucus. Lect Sci Basis Med 8: 235-55, 1959. A 178

REIMANN H A: Acute respiratory tract infections in the aged. Geriatrics 22: 160-67, 1967. A 179

ROSE B and PHILLS J A: The immune reaction in pulmonary disease. Arch Environ Health 14: 97-110, 1967. A 180

ROSS C A C, McMICHAEL S, EADIE M B, LEES A W, MURRAY E A, and PINKERTON I: Infective agents and chronic bronchitis. Thorax 21: 461-64, 1966. A 181

SCHMIDT O-P: Chronische Tabakrauch-Inhalation und Erkrankungen der Atemwege unter Berücksichtigung des Rauchens von Jugendlichen. Munch Med Wochenschr 104: 1832-36, 1962. A 182

SCHMIDT O P: Prophylaxe des chronischen bronchitischen Syndroms. Med Welt 22: 1416-7, 1968. A 183

STUART-HARRIS C: Infection, the environment and chronic bronchitis. J Roy Coll Phys Lond 5: 351-61, 1971. A 184

TRINQUET G and MEYER A: Role de l'oxyde de carbone dans le transfert de l'oxygène au cours des bronchopathies obstructives. Le Poumon et le Coeur 27: 695-704, 1971. A 185

Additional Bibliographic List No. 7

BRONCHIAL CARCINOMA

Reprint

AMERICAN CANCER SOCIETY, INC and NATIONAL CANCER INSTITUTE U S PUBLIC HEALTH SERVICE: Discussion. In: Proceedings of the Fourth National Cancer Conference. J B Lippincott Co., Philadelphia 323-33, 1960. A 186

ANONYMOUS: Malignant cells in sputum. 6, 1972. A 187

BEDROSSIAN C W M: Coexistent emphysema and bronchogenic carcinoma. Cancer Bull 24: 102-7, 1972. A 188

BERNIER J L: Tumors of the lips. In: Tumors of the Oral Regions. Edited by H B G Robinson, W B Saunders Co., Philadelphia, 19-28, 1957. A 189

BLUMBERG B S: Common viruses and their relation to cancer etiology. Cancer Bull 21: 83-5, 1969. A 190

BLUNDI E: A Batalha Do Cancer Do Pulmao. Brasil Med 83: 198-205, 1969. A 191

BONSI R: Dati recenti sull'attivita cancerigena del tabacco. 566-577, A 192

BRYSON G and BISCHOFF F: The limitations of safety testing. In: Progress in Experimental Tumor Research, Edited by F Homburger, S. Karger, New York, 100-33, 1969. A 193

COSIO VILLEGAS I: La prevencion del cancer pulmonar. Neumol Cir Torax 27: 359-65, 1966. A 194

CLOUTIER J P: La lutte contre le cancer au Quebec. Laval Med 38: 421-23, 1967 A 195

DELARUE N C: Cigarette smoking and lung cancer. Appl Ther 4: 919-25, 1962. A 196

FOITZIK E, STAEMMLER M and POSZICH G: Experimental pulmonary carcinomas in albino mice after intranasal infection with influenza virus A_2 Asia. Z Krebsforschung 77: 77-82, 1972. A 197

GSELL OR: Epidemiology of bronchial carcinoma in a mountain region. Oncology 25: 410-14, 1971. A 198

HAMMOND E C: Epidemiologic features of cancer of the lung. In: Cancer Management, sponsored by American Cancer Society, Inc. J B Lippincott Co, Philadelphia, 453-58, A 199

HAMMOND E C: Evolution of concepts concerning etiology and pathogenesis of cancer. Industr Med Surg 37: 616-20, 1968. A 200

HAMMOND E C: Cancer prevention and competitive risks. Arch Environ Hlth 19: 395-402, 1969. A 201

HEALY T M: Carcinoma of the lung: 352 cases. Irish J Med Sci 140: 564-71, 1971. A 202

HYATT C L: Physicians and smoking. J Arkansas Med Soc 184, A 203

KOURILSKY R, HAPPERT J C and FREDY D: Donnees Experimentales sur L'Action Cancérigene Bronchopulmonaire Du Tabac. Bronches 16: 370-80, 1966. A 204

KREYBERG L: Actiology of Cancer. Universitetsforlaget, Oslo, 1-90, 1969. A 205

LANGSTON, H T: Lung cancer--future projection. J Thorac Cardiovasc Surg 63: 412-15, 1972. A 206

LEUCHTENBERGER C and LEUCHTENBERGER R: Effects of chronic inhalation of whole fresh cigarette smoke and of its gas phase on pulmonary tumorigenesis in Snell's mice. In: Morphology of Experimental Respiratory Carcinogenesis, Sponsored by National Cancer Institute and U. S. Atomic Energy Commission, 329-46, 1970. A 207

MEINSMA L: Roken en Longcarcinoom. Ned Tijd Genees 111: 233-34, 1967. A 208

MENDEZ F L, Jr., MAURER E R P and FRECKMAN H A: Effect of chemical agents on bronchogenic cancer. Arch Surg 87: 147-53, 1963. A 209

MORGAN J M: Hepatic copper, manganese, and chromium content in bronchogenic carcinoma. Cancer 29: 710-13, 1972. A 210

OVERHOLT RH: The challenge of pulmonary carcinoma. Delaware Med J 33: 63-67, 1961. A 211

OVERHOLT R H: Primary carcinoma of the lung. CA 17: 262-67, 1967. A 212

OVERHOLT R H, OLIYNYK P N and CADY B: The current status of primary carcinoma of the lung. In: Progress in Clinical Cancer, Edited by I M Ariel, Grune and Stratton, New York IV: 211-22, 19 . A 213

RASMUSSEN R A, BASINGER C E, HARRISON R W and MEADE R H: Choice of operation in the treatment of bronchogenic carcinoma. Dis Chest 46: 190-7, 1964. A 214

RIGDON R H and KIRCHOFF H: Cancer of the lung 1930 to 1960. A review. Texas Rept. Biol. Med. 19: 465-513, 1961. A 215

RIGGINS H M: Primary lung cancer: present and future. A 216

ROBERTSON L S: The National Cancer Association of South Africa. S. African Cancer Bull 14: 119-24, 1970. A 217

ROSS, C A: Cigarette smoking and cancer of the lung. Geriatrics 23: 179-80, 1968. A 218

SPAIN D M: The distribution of tracheobronchial metaplasia (regenerative hyperplasia) (age, sex, cigarette smoking and relation to reid index--preliminary report). In: Current Research in Chronic Respiratory Disease, Proceedings 11th Aspen Emphysema Conference, Aspen Colorado, June 12-15, 1968, 183-186, 1963. A 219

STASZEWSKI J: Palenie a Rak Wargi, Jamy Ustnej, Migdalkow I Krtani. Nowotwory 20: 121-32, 1960. A 220

TOKUHATA, GK: Cancer of the lung: host and environmental interaction. Penna Dept. of Hlth. 1-48, 1972. A 221

VAN DER WAL AM, HUIZINGA E, ORIE N G M, SLUITER H J and DE VRIES K: Cancer and chronic non-specific lung disease (CNSLD). Scand J. Resp. Dis 47: 161-172, 1966. A 222

WYNDER E L and HOFFMANN D: The epidermis and the respiratory tract as bioassay systems in tobacco carcinogenesis. Brit J Cancer 24: 574-87, 1970. A 223

AIR POLLUTANTS AND LUNG DISEASE

	Reprint
ADAMS A I: The stresses of urban living. Health 19: 12-15, 1969.	A 224
ANDERSON D O: The effects of air contamination on health. Canad Med Ass J 97: 528-36, 1967.	A 225
ANDERSON D O: The effects of air contamination on health. Part II Canad Med Ass J 97: 585-93, 1967.	A 226
ANDERSON D O and FERRIS B G, Jr.: Community studies of the health effects of air pollution--a critique. Canad J Pub Health 57: 209-220, 1966.	A 227
AYRES S M and BUEHLER M E: The effects of urban air pollution on health. Clin Pharmacol Ther 11: 337-71, 1970.	A 228
BALCHUM O J: Environment in relation to respiratory disease. Arch Environ Hlth 4: 561-74, 1962.	A 229
BATES D V: Air pollutants and the human lung. Amer Rev Resp Dis 105: 1-13, 1972.	A 230
BEERENS J: Pollution de l'air luchtverontreiniging. Acat Tuber Pneumol 53: 429-48, 1967.	A 231
BRODINE V: Point of damage. Environment 14: 2- 15, 1972.	A 232
CAREY G C R, PHAIR J J, SHEPHARD R J and THOMSON: The effects of air pollution on human health. Amer Industr Hyg Ass J 19: 363-70, 1958.	A 233
CASARETT L J: Toxicology: The respiratory tract. Ann Rev Pharm 11: 425-46, 1971.	A 234
DE LOURDES FONSECA SANTOS M: Aspectos clinicos das Doencas Broncopulmonares de Causa Inalatioria. Jornal do Medico 77: 143-49, 1971.	A 235
DEVILLIERS, A: The effects of air pollution on health. Occup. Hlth Rev 20: 25-44, 1968-1969.	A 236
ECKARDT R E: Air pollution, lung cancer, and chronic lung disease. J Occup Med 6: 184-8, 1964.	A 237
FERRIS B G: Eipidemiological studies on air pollution and health. Arch Environ Hlth 16: 541-55, 1968.	A 238
FERRIS B G and WHITTENBERGER J L: Environmental hazards. Effects of community air pollution on prevalence of respiratory disease. New Engl J Med 275: 1413-19 1966.	A 239
GOLDSMITH J R: The new airborne disease. Calif Med 113: 13-20, 1970.	A 240
GOLDSMITH J R, GREENBURG L, ALTSHULLER, A P, SPICER W S, CASSELL E J, and LANDSBERG H E: Amer Rev Resp Dis 93: 302-12, 1966.	A 241
GROSS P: The pulmonary reaction to man's environment. 106-11,	A 242
HAMMOND E C: Epidemiological evidence on the effects of air pollution. 60th Annual Meeting Air Pollution Control Association, Cleveland, Ohio, June 14, 1967.	A 243
HAMMOND E C: Testimony. Before the Subcommittee on Air and Water Pollution of the Senate Committee on Public Works, July 30, 1968.	A 244

List No. 8

Reprint

HEIMANN H: Effects of air pollution on human health. WHO Monogr Ser. No. 46: 159-220, 1961. A 245

HEIMANN H: Status of air pollution helath research, 1966. Arch Environ Hlth 14: 488-503, 1967. A 246

HIGGINS I T T: Air pollution and chronic respiratory disease. Ashrae J 8: 37-45, 1966. A 247

INGRAHAM H S: Respiratory disease and air pollution. 4-17, A 248

KOTIN P: Opportunities in environmental and occupational pathology. Lab Invest 13: 619-23, 1964. A 249

LINDALL A W: Effect of air pollution from fossil fuel combustion on human health. Minnesota Med 321-26, 1970. A 250

MOTLEY H L and PHELPS H W: Pulmonary function impairment produced by atmospheric pollution. Dis Chest 45: 154-62, 1964. A 251

OCHSNER A: The hazards of air pollution fact or fiction? . Med Tribune, March 11 and 14, 1967. A 252

PRINCI, F: Air pollution --facts and fable. J Occup. Med 461-67, 1963. A 253

REICHEL G: Umwelteinflusse and obstruktive atemerkrankungen. Schweiz Med Wschr 102: 102-9, 1972. A 254

SALATA J R: Air pollution. Rocky Mount Med J 63: 47-51, 1966. A 255

SPICER W S, Jr.: Relation of air pollution to disease. Arch Environ Hlth 9: 600-5, 1964. A 256

SPOTNITZ M: Air pollution respiratory syndromes: A military medical problem. Milit. Med 131: 1499-1503, 1966. A 257

STRESEMANN E: The medical and biological importance of exhaust gases from motor vehicles. Staub-Reinhalt Luft 29: 11-16, 1969. A 258

WALLER RE: Air pollution and community health. J Roy Coll Physicians Lond 5: 362-8, 1971 . A 259

WINKELSTEIN W, Jr. and FRENCH F E: The role of ecology in the design of a health care system. Calif Med 113: 7-12, 1970. A 260

Additional Bibliographic List No. 9

PULMONARY EMPHYSEMA-BRONCHITIS COMPLEX: ETIOLOGY & PATHOLOGY

Reprint

ANDERSON D O: Chronic nontuberculous respiratory diseases. In: Preventive Medicine, edited by Duncan W Clark and Brian MacMahon, Little, Brown and Company, Boston, 491-507, A 261

ANONYMOUS: The nature of chronic bronchitis and emphysema. NTA Bulletin :7-12, 1967. A 262

BARCLAY W R: Axioms on chronic pulmonary disease. Hosp Med 5: 70-1, 75-9, 1969. A 263

BATES D V: Chronic bronchitis and emphysema. New Engl J Med 278: 546-51, 1968. A 264

BATES D V: Chronic bronchitis and emphysema (concluded). New Engl J Med 278: 600-5, 1968. A 265

BURROWS B, FLETCHER C M, HEARD B E, JONES N L and WOOTLIFF J S: The emphysematous and bronchial types of chronic airways obstruction. A clinico-pathological study of patients in London and Chicago. Lancet 1: 830-5, 1966. A 266

BURROWS B and KETTEL L J: Important considerations in emphysema-chronic bronchitis syndrome. Geriatrics 24(11): 72-82, 1969. A 267

COHEN B M: When to suspect that masquerading malady: obstructive lung disease. Consultant 7: 32-6, 1967. A 268

DAVID W: Chronic respiratory diseases — the new look in the public health service. Am J Public Health 57: 1357-62, 1967. A 269

EBERT R V: Chronic bronchitis and pulmonary emphysema. Postgrad Med 29: 341-5, 1961. A 270

FLETCHER C M: Discussion on bronchitis and emphysema. Practitioner 188: 403-5, 1962. A 271

FLETCHER C M: Bronchitis and emphysema. Proc Roy Soc Med 55: 451-3, 1962. A 272

FLETCHER C M: Bronchitis-emphysema syndrome. Disease-a-Month December: 1-48, 1963. A 273

FRUHMANN G Exogene und endogene Faktoren in der Ätiologie chronisch-unspezifischer Atemwegerkrankungen. Med Klinik 63: 1288-95, 1968. A 274

HARTUNG M: Die Klinik der chronischen unspezifischen Atemwegsyndrome. Zugleich ein Beitrag zur klinischen Diagnostik und Klassifizierung. Med Klinik 63: 1296-1302, 1968. A 275

HARTUNG W: Pathologische Anatomie und Pathogenese der Bronchitis und des Emphysems. Internist 10(4): 121-32, 1969. A 276

HOLLAND W W: Chronische bronchitis und lungenemphysen. In: Nikotin, edited by Helmut Schievelbein, Georg Thieme Verlag, Stuttgart, 230-41, 1968. A 277

HUNT JR W B: Criteria for diagnosis of asthma, chronic bronchitis and emphysema. With

List No. 9

	Reprint
KINSELLA T J: The indeterminate lung lesion. J Lancet 82: 27-34, 1962.	A 279
LARSEN K A: Patologisk anatomi og patogenetiske faktorer. Läkartidningen 67: 375-83, 1970.	A 280
MARX H H: Die emphysembronchitis. Dtsch Med Wochenschr 96: 833-8, 1971.	A 281
MENEFEE JR E E: Bronchitis and emphysema. Virginia Med Monthly 84: 53-6, 1957.	A 282
MITCHELL R S: The fight against chronic non-specific respiratory diseases. In: Bronchitis, edited by N G M Orie and H J Sluiter, Royal Vangorcum, Assen, Netherlands and Charles C Thomas, 343-52, 1964.	A 283
MITCHELL R S, SILVERS G W, DART G A, PETTY T L, VINCENT T N, RYAN S F and FILLEY G F: Clinical and morphologic correlations in chronic airway obstruction. Am Rev Resp Dis 97: 54-61, 1968.	A 284
MORGAN W K: Irreversible obstructive airway disease: definition, pathology and etiology. West Va Med J 64: 288-92, 1968.	A 285
MULLER H: Chronic bronchitis and emphysema. S Afr Med J 33: 805-7, 1959.	A 286
OSWALD N C: The clinical importance of recent advances in bronchitis and emphysema. Postgrad Med 35: 233-6, 1964.	A 287
PRATT P C and THONG-YAI K: The relative importance of bronchiolitis and extent of centrilobular emphysema in pulmonary ventilatory interference. Public Health Service Publication No. 1787: 339-55, 1968.	A 288
PUGSLEY H E: The underwriting of chronic pulmonary diseases. Proc ALC Med Section : 106-16,	A 289
RAPPAPORT I and MAYER E: Changing forms and causes of pulmonary insufficiency in present era of medicine. J Am Med Ass 165: 431-6, 1957.	A 290
TAUB S J: Emphysema, chronic bronchitis and asthma. Eye Ear Nose Throat Monthly 45: 110-2, 1966.	A 291
THURLBECK W M: Chronic obstructive lung disease. : 367-98,	A 292
THURLBECK W M and ANGUS G E: The relationship between emphysema and chronic bronchitis as assessed morphologically. Am Rev Resp Dis 87: 815-9, 1963.	A 293
THURLBECK W M, HENDERSON J A, FRASER R G and BATES D V: Chronic obstructive lung disease. A comparison between clinical, roentgenologic, functional and morphologic criteria in chronic bronchitis, emphysema, asthma and bronchiectasis. Medicine 49: 81-145, 1970.	A 294
TURNER W A: Chronic obstructive lung disease. Nova Scotia Med Bull 48: 3-11, 1969.	A 295
VALENTIN H and WOITOWITZ H-J: Chronische Bronchitis und Lungenemphysem als arbeitsmedizinisches Problem. Internist 8: 165-72, 1967.	A 296
VOISIN C: Les facteurs etiologiques dans la bronchite chronique et l'emphysème pulmonaire. La Revue de Medecine 11: 2175-9, 1970.	A 297
WESSEL-AAS T: Obstruktive Lungesykdommer. Tidsskr Nor Laegeforen 87: 566-8, 1967.	A 298

Additional Bibliographic List No. 10

PULMONARY EMPHYSEMA-BRONCHITIS COMPLEX: CLINICAL STUDIES

	Reprint
ASTIN T W: Reversibility of airways obstruction in emphysema. Lancet 1: 1128, 1972.	A 299
BARACH A L, CHUSID E L and WOOD L: Ventilatory effect of decreasing functional residual capacity in pulmonary emphysema. Ann Allergy 25: 211-23, 1967.	A 300
BROCARD H: Poumon et travail; exposé de synthèse. CAMIP 35-36: 88-94, 1969.	A 301
BROWN E A: The pulmonary cripple. Mississippi Valley Med J 80: 80-5, 1958.	A 302
BURROWS B: Chronic obstructive lung disease. (Bronchitis-emphysema syndrome) Diagnosis and physiologic effects. Postgrad Med 39: 105-12, 1966.	A 303
BURROWS B: The course of patients with chronic obstructive lung disease. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education and Welfare, Public Health Service Publication No. 1879: 253-8, 1969.	A 304
CARABASI R J: Asthma? Bronchitis? Emphysema? A diagnostic dilemma. Postgrad Med 39: 553-5, 1966.	A 305
DALY W J: Single-breath gas distribution in chronic obstructive lung disease. Arch Intern Med 127: 763-6, 1971.	A 306
DINES D E: Monitoring certain aspects of respiratory failure. Dis Chest 54: 421-6, 1968.	A 307
EARLE R H and BURROWS B: Prognosis in chronic obstructive lung disease. Public Health Service Publication No. 1787: 453-62, 1972.	A 308
FARCON E M and MORALES P A: The association of chronic obstructive pulmonary disease (COPD) and lower urinary tract symptoms. J Urology 108/4: 619-22, 1972.	A 309
FILLEY G F: Emphysema and chronic bronchitis: clinical manifestations and their physiologic significance. Med Clin N Amer 51: 283-92, 1967.	A 310
FLETCHER C M, HUGH-JONES P, McNICOL M W and PRIDE N B: The diagnosis of pulmonary emphysema in the presence of chronic bronchitis. Quart J Med 32: 33-47, 1963.	A 311
GONZALEZ E, WEILL H, ZISKIND M M and GEORGE R B: The value of the single breath diffusing capacity in separating chronic bronchitis from pulmonary emphysema. Dis Chest 53: 229-36, 1968.	A 312
HARRIS H W: Chronic bronchitis, emphysema, and asthma. Amer J Pub Health 53 suppl. P+II: 7-15, 1963.	A 313
HEPPER N G, BLACK L F, DINES D E and MILLER R D: The concept of an emphysema clinic. Mayo Clin Proc 43: 306-10, 1968.	A 314

HERZOG H: Chronisch-obstruktive Lungenerkrankungen. Pathophysiologie, Klinik und

List No. 10 Reprint

HOGG J C, MACKLEM P T and THURLBECK W M: The resistance of small airways in normal and diseased human lungs. Public Health Service Publication No. 1787: 433-41, 1972. A 316

HUTTNER I and HUTTNER H: Die Motivation des Gesundheitsverhaltens. Teil I. Zschr ärztl Fortbild 64: 471-7, A 317

KRUMHOLZ R A: A comprehensive respiratory disease program. Ohio St Med J 65: 147-9, 1969. A 318

LORD G P, GAZIOGLU K and KALTREIDER N: The maximum expiratory flow-volume in the evaluation of patients with lung disease. Am J Med 46: 72-9, 1969. A 319

MARX H H: Gesichtspunkte zur Begutachtung der primär oder sekundär unspezifischen Lungenkrankheiten. Beitr Klin Tuberk 136: 172-8, 1966. A 320

MOLHO M, RAZ I and KREISLER B: A basis for differentiating between primary emphysema and pulmonary obstruction disease due to chronic bronchitis. :29-35, A 321

MORTON J W and TURNBULL K W: The reversibility of chronic bronchitis, asthma and emphysema. Dis Chest 53: 126-32, 1968. A 322

PENMAN R W and ASTIN T W: Airway obstruction due to hypoxemia in patients with chronic lung disease. Public Health Service Publication no. 1787: 145-59, 1968. A 323

PENMAN R W, O'NEILL R P and BEGLEY L: The progress of chronic airway obstruction in relation to measurements of airway resistance and lung elastic recoil. Am Rev Resp Dis 101: 536-44, 1970. A 324

PIERCE J A: Office management of chronic obstructive pulmonary disease. Clin Notes Resp Dis 7: 3-11, 1968. A 325

PIRCHER F J: Lung scanning in the assessment of obstructive lung disease. Public Health Service Publication No. 1787: 429-31, 1972. A 326

PISTAWKA H J: Chronic airway obstruction. Current Therap : 99-104, 1969. A 327

SIERING H: Bronchitis, Peribronchitis und Emphysem. Zschr ärztl Fortbild 60: 602-8, A 328

SUFRIN M: To screen or not to screen for COPD. Bull Nat Tuberc Resp Dis Ass 56: 11-13, 1970. A 329

SUKUMALCHANTRA YOSVI and WILLIAMS JR M H: Serial studies of pulmonary function in patients with chronic obstructive pulmonary disease. Am J Med 39: 941-5, 1965. A 330

TECULESCU D and RACOVEANU C: A clinical roentgenologic and biologic classification of patients with chronic obstructive lung disease. Rev Roum Med Int 9: 39-50, 1972. A 331

THURLBECK W: The pathological anatomy of chronic obstructive lung disease. J Clin Pathol 24: 482, 1971. A 332

TYSINGER JR D S: Pulmonary function testing for the general hospital and physician. J Med Ass Alab 39: 834-40, 1970. A 333

VARGHA G: Eine neue - auf die Bronchiale Schleimdrüsenhyperplasie Gegründete - Entstehungstheorie für das Obstruktive Emphysem. Acta Med Acad Scient Hung 26: 73-8, 1969. A 334

Additional Bibliographic List No. 11

MORBIDITY STUDIES

Reprint

ANON: The ethnic distribution of disease in the United States. J Chron Dis 20: 115-18, 1967. A 335

ANON: Zur bedeutung chronisch-inhalativer noxen am arbeitsplatx fur chronische bronchitis und lungenemphysem (The significance of chronic inhalable noxae at the place of work for chronic bronchitis and pulmonary emphysema). Munch Med Wochenschr. 113: 1302-7, 1971. A 336

ASHFORD J R, BROWN S, MORGAN D. C and RAE S: The pulmonary ventilatory function of coal miners in the United Kingdom. Am Rev Resp Dis 97: 810-21, 1968. A 337

BAKER T R, OSCHERWITZ M, CORLIN R, JARBOE T, TEISCH J and NICHAMAN MZ: Screening and treatment program for mild chronic obstructive pulmonary disease. JAMA 214: 1448-1455, 1970. A 338

BERNDT V H: Bronchialkarzinom und ulcus pepticum. Med Klin 57: 1397-1401, 1962. A 339

BLACK L F and HYATT R E: Maximal static respiratory pressures in generalized neuromuscular disease. Am Rev Resp Dis 103: 641-50, 1971. A 340

BROWN K E and CAMPBELL A H: Tobacco, alcohol and tuberculosis Br J Dis Chest 55: 150-8, 1961. A 341

BURNS M W and MAY J R: Haemophilus influenzae precipitins in the serum of patients with chronic bronchial disorders. Lancet 1: 354-58, 1967. A 342

CALIFORNIA MEDICAL ASSOCIATION: The smoking study. Calif Med 109: 339-44, 1968. A 343

CHERNIACK N S, DOWLING H F, CARTON R W, and McBRYDE V E: The role of acute lower respiratory infection in causing pulmonary insufficiency in bronchiectasis. Ann Intern Med 66: 489-97, 1967. A 344

COHEN A C and JENNEY F S: The frequency of peptic ulcer in patients with chronic pulmonary emphysema. Am Rev Resp Dis 85: 130-32, 1962. A 345

CONALLY N T: Early detection of disease in young men. Med Ann DC 38: 672-76, 1969. A 346

CUNNINGHAM D A, MONTOYE H J, HIGGINS M W and KELLER J B: Smoking habits, chronic bronchitits and shortness of breath and physical fitness. Med Sci Sports 4: 138-45, 1972. A 347

D'ANELLI A, PROSCIA N, SORISTO F and CARATTI C A: L'enfisema polmonare cronico ostruttivo nel malato ulceroso (Chronic obstructive emphysema in the ulcer patient). Arch Sc Med 17: 191-94, 1965. A 348

DeMARRAIS G A: The meteorology associated with New Orleans asthma. Arch Environ Health 11: 787-93, 1965. A 349

List No. 11 — Reprint

DOYLE J T: Cigarette smoking. Minn Med 1311-13, 1969. — A 350

ENTERLINE P E: The effects of occupation on chronic respiratory disease. Arch Environ Health 14: 189-200, 1967. — A 351

FERRIS B G Jr, ANDERSON D O and BURGESS W A: Prevalence of respiratory disease in a flax mill in the United States. Br J Ind Med 19: 180-85, 1962. — A 352

GOLDSMITH J R: Epidemiology of bronchitis and emphysema. Medicina Thoracalis 22: 1-23, 1965. — A 353

GOLDSMITH J R and DEANE M: Outdoor workers in the United States and Europe. Milbank Mem Fund Q 43: 107-16, 1965. — A 354

GOTTSCHING V H and GOTTSCHING C: Uber haufigkeit, pathogenese und verlauf der progressiven lungendystrophie. Prax Pneumol 20: 92-105, 1966. — A 355

GREENBERG M, MILNE J F and WATT A: Survey of workers exposed to dusts containing derivatives of Bacillus Subtilis. Bull Med J 2: 629-33, 1970. — A 356

GREGG I: The identification of the early stages of chronic bronchitis. Medicina Thoracalis, 24: 77, 1967. — A 357

GUPTA S, PURI R K, INDIRA O C and DATTA S P: Morbidity in children under fourteen in South India. Indian Pediatr 5: 485-97, 1968. — A 358

HARRISON T R and REEVES T J: Stress, diet, drugs and habits. In: Principles and Problems of Ischemic Heart Disease, Year Book Publishers, Chicago, pp 148-60, 1968. — A 359

HAUSKNECHT R: Experiences of a respiratory disease panel selected from a representative sample of the adult population. Am Rev Resp Dis 86: 858-66, 1962. — A 360

HERXHEIMER H and HOLMSTEDT B: Atropinzigaretten bei asthma und emphysem. 37: 957-62, 1959. — A 361

HOLDAWAY M D and TURK D C: Capsulated haemophilus influenzae and respiratory-tract disease. Lancet 1: 358-60, 1967. — A 362

HOLLAND W W: A respiratory disease study of industrial groups. Arch Environ Health 6: 9-16, 1963. — A 363

HORN D and WAINGROW S: Some dimensions of a model for smoking behavior change. Am J Public Health 56: 21-26, 1966. — A 364

JAMES G: Emerging trends in public health and possible reactions. Public Health Reports 80: 579-86, 1965. — A 365

KENDIG E L: Chronic respiratory diseases in children. Minn Med 52: 1363-67, 1967. — A 366

KLEIN R C, SALVAGGIO J E and KUNDUR V G: The response of patients with "idiopathic" obstructive pulmonary disease and "allergic" obstructive bronchitis to prednisone. Ann Intern Med 71: 711-78, 1969. — A 367

KUPKA E and GOLDSMITH J R: Crossing of the curves II: Tuberculosis and Emphysema. Dis Chest 41: 514-17, 1962. — A 368

List No. 11 — Reprint

LEMLE A, VIEIRA L O B D, MILWARD G A F and MIRANDA J L: Lung function studies in pulmonary South American blastomycosis. Am J Med 48: 434-42, 1970. — A 369

MATHOV E: Complicaciones del asma bronquial. El Dia Medico (4 Dec 1969), pp 2806-10. — A 370

McKEE W D: Environmental problems and the allergist. Ann Allergy 29: 510-24, 1971. — A 371

MEDICAL RESEARCH COUNCIL: Value of chemoprophylaxis and chemotherapy in early chronic bronchitis. Bull Med J 1: 1317-22, 1966. — A 372

MERRILL M H: Public health responsibilities and program possibilities in chronic respiratory diseases. Am J Public Health 53: 25-33, 1963. — A 373

MILLER G J and SERJEANT G R: An assessment of lung volumes and gas transfer in sickle-cell anemia. Thorax 26: 309-15, 1971. — A 374

MILLS M and BAISCH B F: Spontaneous pneumothorax. Ann Thorac Surg 1: 286-97, 1965. — A 375

MOFFAT M A J and SUTHERLAND J A W: Persistence of viral antibodies in patients with chronic bronchitis. Br Med J 1: 601-603, 1967. — A 376

MONSON R R: Duodenal ulcer as a second disease. Gastroenterology 59: 712-16, 1970. — A 377

OTTO H and HINUBER G V: Zur haufigkeit des emphysema, der tuberkulose und des bronchuskarzinoms bei staublungenerkrankungen. (The incidence of emphysema and bronchogenic carcinoma in silicosis). Prax Pneumol 26: 145-58, 1972. — A 378

PALMER K N V and DIAMENT M L: A comparison of pulmonary function in bronchial asthma and chronic obstructive bronchitis. Thorax 25: 101-4, 1970. — A 379

PERALES G M G: Simposio sobre problemas medicos originados por el tabaquismo. Alteraciones morfologicas en diferentes organos y sistemas. Neumol Cir Thorax Mex 32: 27-29, 1971. — A 380

PHILLIPS A M, PHILLIPS R W and THOMPSON J L: Chronic cough: analysis of etiologic factors in a survey of 1,274 men. Ann Intern Med 45: 216-231, 1956. — A 381

PHILLIPS J R: Gastroduodenal ulceration in chronic obstructive lung diseases. J Abdominal Surg 8: 306-7, 1966. — A 382

SCHUMAN L M: Epidemiologic approaches and problems in the assessment of causal factors in chronic respiratory disease. J Kentucky Med Ass 64: 311-16, 1966. — A 383

SCHUNEMANN V G: Die betreuung der patienten mit einem chronisch bronchitischen syndrom in der kreisstelle fur tuberkulose und lungenkrankheiten rostock. Z. Ges Ann Med 25: 352-55, 1970. — A 384

SILEN W, BROWN W H and EISEMAN B: Peptic ulcer and pulmonary emphysema. Arch Surg 78: 897-903, 1959. — A 385

STEBBINGS J H Jr: A survey of respiratory disease among New York City postal and transit workers. III. Anthropometric, smoking, occupational, and ethnic variables affecting the FEV_1 among white males. Environ Res 5: 451-66, 1972. — A 386

List No. 11 Reprint

STEBBINGS J H Jr: Two observed associations between respiratory and hypertension in nonsmokers. Am J Epidemiol 97: 4-15, 1973. A 387

STEWART G T: Epidemiological approach to assessment of health. Lancet 2: 115-19, 1970. A 388

WALKER I C: The treatment of patients with bronchial asthma with subcutaneous injections of the proteins to which they are sensitive. J Med Res 36: 423-80, 1917. A 389

WEHRLE P F, BRENT R L, DOYLE J L, FARR L E, FAGAN E L, FINBERG L, NAHMIAS A J, PICKERING D E and YAMAZAKI J N. Smoking and children: A pediatric viewpoint. Pediatrics 44: 757-59, 1969. A 390

WEST W O, BURNS R O, DANIEL J M and JACKSON H A: The Syndrome of chronic pulmonary disease and gastroduodenal ulceration. Arch Intern Med 103: 897-901, 1959. A 391

WYNDER E L, LEMON F R and MANTEL N: Epidemiology of persistent cough. Am Rev Resp Dis 91: 679-700, 1965. A 392

SYNDER E L, LEMON F R and MANTEL N: La epidemiologia de la tos persistent. Folia Clinica Intern 15: 78-88, 1965. A 393

ZASLY L, BAUM G L and RUMBALL J M: The incidence of peptic ulceration in chronic obstructive pulmonary emphysema. Dis Chest 37: 400-5, 1960. A 394

INDUSTRIAL HAZARDS

Reprint

AHEARN V P, SANDER O A, VORWALD A J, WRIGHT G W and HARTMAN W C: Emphysema pneumoconioses and compensation. Arch Environ Health 2: 307-26, 1961. A 395

AMDUR M O: Respiratory absorption data and SO_2 dose-response curves. Arch Environ Health 12 (6): 729-32, 1966. A 396

AYER H E and LYNCH J R: Association of disability and selected occupational hazards. Arch Environ Health 17: 225-31, 1968. A 397

BALCHUM O J, DYBICKI J and MENEELY G R: The dynamics of sulfur dioxide inhalation. Arch Indust Health 21: 564-9, 1960. A 398

BALLENGER J J, McFARLAND C R, HARDING H B, KOLL M and HALSTEAD D: The effect of air pollutants on pulmonary clearance. Laryngoscope 78: 1387-97, 1968. A 399

BOUHUYS A and PETERS J M: Control of environmental lung disease. New Engl J Med 283: 573-82, 1970. A 400

CARNOW B, LEPPER M H, SHEKELLE R B and STAMLER J: Chicago air pollution study. Arch Environ Health 18: 768-76, 1969. A 401

CHESTER E H, GILLESPIE D G and KRAUSE F D: The prevalence of chronic obstructive pulmonary disease in chlorine gas workers. Am Rev Resp Dis 99: 365-73, 1969. A 402

DEICHMANN W B, KITZMILLER K V and WITHERUP S: Phenol studies VII. Chronic phenol poisoning with special reference to the effects upon experimental animals of the inhalation of phenol vapor. Am J Clin Pathol 14: 273-7, 1944. A 403

DEICHMANN W B, WITHERUP S and DIERKER M: Phenol studies XII. The percutaneous and alimentary absorption of phenol by rabbits with recommendations for the removal of phenol from the alimentary tract or skin of persons suffering exposure. J Pharmacol Exp Ther 105: 265-72, 1952. A 404

DISCHER D P, MASSEY F J and WALLACE R R: Screening by chest photofluorography in Los Angeles. The minifilm circa 1970. Arch Environ Health 22: 92-105, 1971. A 405

ENTERLINE P E: Epidemiology of coal workers' pneumoconiosis. Indust Med 39: 20-2, 1970. A 406

FORBES J D: Cutting and grinding fluids in chronic pulmonary airway disease. J Occup Med 9/8: 421-3, 1967. A 407

FURLANETO J A, ANDERSON A E and FORAKER A G: Soot emphysema in a locomotive engineer. Arch Environ Health 18: 1008-13, 1969. A 408

GOFF A M and GAENSLER E A: Asbestosis following brief exposure in cigarette filter manufacture. Respiration 29/1: 83-93, 1972. A 409

GREEN H L: Respiratory protection against particulates -- problems solved and unsolved. Am Indust Hyg Assoc 26: 203-11, 1965. A 410

GRIMLEY K W, ADAMS C N and WALTON R A: Screening for chronic pulmonary disease--the Alabama experience. Am J Pub Health 59: 1188-98, 1969. A 411

List No. 12 — Reprint

GROSS P: Some aspects of pneumoconiosis. Pathol Annu 6: 61-79, 1971. — A 412

HACKETT R L and SUNDERMAN F W: Pulmonary alveolar reaction to nickel carbonyl. Arch Environ Health 16: 349-61, 1968. — A 413

HALLETT W Y: Effect of ozone and cigarette smoke on lung function. Arch Environ Health 10: 295-302, 1965. — A 414

HEINRICHS E H and HINS B F: Emphysema rehabilitation program in South Dakota. S Dakota J Med 21: 31-3, 1968. — A 415

HEPPER N G, HYATT R E and FOWLER W S: Detection of chronic obstructive lung disease. Arch Environ Health 19: 806-13, 1969. — A 416

HEPPLESTON A G: Emphysema in relation to dust exposure. In: Pneumoconiosis. Proceedings of the International Conference, Johannesburg 1969, edited by H A Shapiro, Cape Town Oxford University Press, London, 312-4, 1970. — A 417

HORTON A W, TYE R and STEMMER K L: Experimental carcinogenesis of the lung. Inhalation of gaseous formaldehyde or an aerosol of coal tar by C_3H Mice. J Nat Cancer Inst 30: 31-43, 1963. — A 418

LEWIS C E and KERBY G R: An epidemic of polymer-fume fever. J Am Med Ass 191: 375-8, 1965. — A 419

LOB M: Pathologie respiratoire professionnelle en dehors de la silicose. Therapeutische Umschau/ Revue thérapeutique 27: 10-6, 1970. — A 420

MORGAN W K: Coal workers' pneumoconiosis. Am Indust Hyg Ass J 32: 29-34, 1971. — A 421

MURPHY R L, FERRIS B G, BURGESS W A, WORCESTER J and GAENSLER E A: Effects of low concentrations of asbestos. Clinical, environmental, radiologic and epidemiologic observations in shipyard pipe coverers and controls. New Engl J Med 285: 1271-8, 1971. — A 422

MURPHY S D, LENG J K, ULRICH C E and DAVIS H V: Effects on animals of exposure to auto exhaust. Arch Environ Health 7: 60-70, 1963. — A 423

NAEYE R L and DELLINGER W S: Coal workers' pneumoconiosis. Correlation of roentgenographic and postmortem findings. J Am Med Assoc 220(2): 223-7, 1972. — A 424

NIDEN A H: Effects of ammonia inhalation on the terminal airways. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 41-4, 1969. — A 425

PATTLE R E and BURGESS F: Toxic effects of mixtures of sulphur dioxide and smoke with air. J Path Bact 73: 411-9, 1957. — A 426

PENMAN R W: A summary of the conclusions from an international conference on coal workers' pneumoconiosis. Am Rev Resp Dis 102: 243-7, 1970. — A 427

SARIC M and GOLDSMITH J R: Methods for investigating the relationship of chronic bronchitis and emphysema to occupational exposures. In: XIVth International Congress of Occupational Health, Volume II, edited by P Sangro, G Akoun, and H L Beale, Excerpta Medica Foundation, Amsterdam, 741-51, 1964. — A 428

STOKINGER H E, WAGNER W D and DOBROGORSKI O J: Ozone toxicity studies. III. Chronic injury to lungs of animals following exposure at a low level. Arch Indust — A 429

List No. 12

Reprint

VIIKERI M, JÄÄSKELÄINEN J and TÄHTI E: Ultrasonic examination of pleural thickenings and calcifications in occupational asbestosis. Dis Chest 54: 17-20, 1968.

A 430

PULMONARY FUNCTIONAL TESTS

Reprint

BEECKMANS J M: The deposition of aerosols in the respiratory tract. II. Deposition in cigarette smoking. Canad J Physiol Pharmacol 43: 707-14, 1965. A 431

BOUHUYS A, GEORG J, JONSSON R, LUNDIN G and LINDELL S-E: The influence of histamine inhalation on the pulmonary diffusing capacity in man. J Physiol 152: 176-81, 1960. A 432

BOUHUYS A, JONSSON R, LICHTNECKERT S, LINDELL S-E, LUNDGREN C, LUNDIN G and RINGQUIST T R: Effects of histamine on pulmonary ventilation in man. Clin Sci 19: 79-94, 1960. A 433

BRISCOE W A and DUBOIS A B: The relationship between airway resistance, airway conductance and lung volume in subjects of different age and body size. J Clin Invest 37: 1279-85, 1958. A 434

BURGER JR E J and MACKLEM P: Airway closure: demonstration by breathing 100% O_2 at low lung volumes and by N_2 washout. J Appl Physiol 25: 139-48, 1968. A 435

CALDWELL E J and FRY D L: Pulmonary mechanics in the rabbit. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 307-20, 1969. A 436

CASARETT L J: Role of radioactive substances in effects of smoking. In: Toward a Less Harmful Cigarette. National Cancer Institute Monograph 28, edited by E L Wynder and D Hoffmann, U.S. Department of Health, Education, and Welfare, Public Health Service, National Cancer Institute, Bethesda, Maryland, 199-209, 1968. A 437

DALHAMN T, EDFORS M-L and RYLANDER R: Retention of cigarette smoke components in human lungs. Arch Environ Health 17: 746-8, 1968. A 438

DAVIES C N: The handling of particles by the human lungs. Brit Med Bull 19: 49-52, 1963. A 439

DuBOIS A B, BOTELHO S Y and COMROE JR J H: A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. J Clin Invest 35: 327-35, 1956. A 440

FERIN J: Pulmonary clearance after deposition of aerosols. Lekarske Prace 5: 5-67, 1966. A 441

GAVRILESCU N, TECULESCU D, STANESCU D and CONSTANTIN I: Pulmonary mechanics in young healthy men normal values for some less frequently used parameters. Int Z Angew Physiol 24: 194-207, 1967. A 442

HALE F C; OLSEN C R and MICKEY JR M R: The measurement of bronchial wall components. Am Rev Resp Dis 98: 978-87, 1968. A 443

HERZOG H, KELLER R, MAURER M, BAUMANN H R and NADJAFI A: The distribution of bronchial resistance in obstructive pulmonary disease and in dogs with artificially induced tracheal collapse. Public Health Service Publication No. 1787: 55-91, 1968. A 444

HYATT R E and WILCOX R E: Extrathoracic airway resistance in man. J Appl Physiol 16: 326-30, 1961. A 445

LaBELLE C W, LONG J E and CHRISTOFANO E E: Synergistic effects of aerosols. Arch Indust Health 11: 297-304, 1955. A 446

List No. 13 Reprint

LANGER G and FISHER M A: Concentration and particle size of cigarette-smoke particles. Arch Indust Health 13: 372-8, 1956. A 447

LOUDON R G: Determinants of expiratory airflow. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 275-85, 1969. A 448

LOUDON R G and SHAW G B: Mechanics of cough in normal subjects and in patients with obstructive respiratory disease. Am Rev Resp Dis 96: 666-77, 1967. A 449

MACKLEM P T: Obstruction in small airways - a challenge to medicine. Am J Med 52: 721-4, 1972. A 450

MAISEL J C, SILVERS G W, MITCHELL R S and PETTY T L: Bronchial atrophy and dynamic expiratory collapse. Am Rev Resp Dis 98: 988-97, 1968. A 451

MELLORS R C: Microscopic localization of tobacco smoke products in the respiratory tracts of animals exposed to cigarette smoke. Proc Am Assoc Cancer Res 2: 325, 1958. A 452

MITCHELL R I: Controlled measurement of smoke-particle retention in the respiratory tract. Am Rev Resp Dis 85: 526-33, 1962. A 453

NADEL J A, SALEM H, TAMPLIN B and TOKIWA Y: Mechanism of bronchoconstriction during inhalation of sulfur dioxide. J Appl Physiol 20: 164-7, 1965. A 454

SAFFIOTTI U, BORG S A, GROTE M I and KARP D B: Retention rates of particulate carcinogens in the lungs. Studies in an experimental model for lung cancer induction. The Quarterly : 10-7, 1964. A 455

SIMONSSON B G, JOCOBS F M and NADEL J A: Role of autonomic nervous system and the cough reflex in the increased responsiveness of airways in patients with obstructive airway disease. J Clin Invest 46: 1812-8, 1967. A 456

WOLFF W A, PURDOM E G and ISENHOWER J A: The use of radioisotopes as tracers in cigarette smoke. N Carolina Med J 15: 159-63, 1954. A 457

Additional Bibliographic List No. 14

CONSTITUENTS OF CIGARETTE SMOKE

Reprint

BALLENGER J J, DAWSON F W, DeRUYTER M G and HARDING H B: Effects of nicotine on ciliary activity in vitro. Ann Otol Rhinol and Laryngol 74: 303-11, 1965. A 458

BAUMBERGER J P: The amount of smoke produced from tobacco and its absorption in smoking as determined by electrical precipitation. J Pharmacol Exp Ther 21: 47-57, 1927. A 459

DAVIS T R, BATTISTA S P and KENSLER C J: Mechanism of respiratory effects during exposure of guinea pigs to irritants. Arch Environ Health 15: 412-9, 1967. A 460

DKURIC D, RAICEVIC P and KONSTANTINOVIC I: Excretion of thiocyanates in urine of smokers. Arch Environ Health 5: 12-5, 1962. A 461

HENION K E: Odor pleasantness and intensity: a single dimension? J Exp Psych 90: 275-9, 1971. A 462

IZARD C: Sur la multiplication du Dunaliella bioculata en présence de phase gazeuse de fumée de cigarette et sur l'obtention de mutations en présence d'acroléine. Compt Acad Sci 265: 1799-1802, 1967. A 463

LARSON R K, FUKUDA P and MURRAY J F: Systemic and pulmonary vascular effects of nicotine in anesthetized dogs. : 556-64, 1964. A 464

RIGDON R H: Effect of tobacco condensate on respiratory tract of white Pekin ducks. Arch Pathol 69: 55-63, 1960. A 465

ROSENKRANTZ H and SPRAGUE R: Biochemical screen to investigate whole smoke and vapor phase effects in mice. Arch Environ Health 18: 917-24, 1969. A 466

SAUNDERS W H: Nicotine stomatitis of the palate. Ann Otol 67: 618-27, 1958. A 467

SCHLOTZHAUER W S and SCHMELTZ I: Non-alkaloidal bases from pyrolysis of tobacco leaf pigment at the approximate burn temperature of a cigarette. Tobacco Science : 32-3, 1967. A 468

STEDMAN R L and MILLER R L: Alkylating activity of cigarette smoke condensate. Chem and Industry 1: 618-9, 1967. A 469

TAUBERGER G: Uber die zentrale Herzvagusaktivierung durch Nikotin. Med Exp 10: 258-66, 1964. A 470

TERRELL J H and SCHMELTZ I: Cigarettes: chemical effects of sodium nitrate content. Science 160: 1456, 1968. A 471

WESTERMARK T: Gaseous ions and their possible role in the etiology of lung cancer and some observations on free charges in cigarette smoke. Acta Med Scand 170 (Suppl. 369): 119-20, 1961. A 472

Additional Bibliographic List No. 15

CARDIOPULMONARY EFFECTS OF CIGARETTE SMOKE

	Reprint
ANON: Cigarettes and atherosclerosis. Practitioner 202(1208): 195-6, 1969.	A 473
BARER G R, HOWARD P and McCURRIE J R: The effect of carbon dioxide and changes in blood pH on pulmonary vascular resistance in cats. Clin Sci 32: 361-76, 1967.	A 474
BOREN H G and KRAHL V E: Ventilatory, neural, and other factors influencing the pulmonary microcirculation of the frog. Bibliotheca Anatomica 7: 86-91, 1965.	A 475
COLLOQUES INTERNATIONAUX DU CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE: Le rôle de la paroi artérielle dans l'athérogenèse. 169: 7-139, 1968.	A 476
CONROY J P: Smoking and the anesthetic risk. Anesth Analg Current Researches 48: 388-400, 1969.	A 477
DENNISON JR A D: Athletics and the heart. J Indiana St Med Ass : 850-5, 1964.	A 478
DOYLE J T: The prevention of coronary heart disease. In: Coronary Heart Disease, edited by Albert N. Brest, F A Davis Company, Philadelphia, 305-16, 1969.	A 479
ECHT R: Estimations of pulmonary surface activity in sedentary and exercised rats. IN: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 323-31, 1969.	A 480
EMMANUEL G E, ROSENBLUTH A, ANSARI I, VILLANO R and CARDUCCI R: Evidence of active alveolar closure in the human lung. IN: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U. S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 287-96, 1969.	A 481
FILLEY G F, BECKWITT H J, REEVES J T and MITCHELL R S: Chronic obstructive bronchopulmonary disease. II. Oxygen transport in two clinical types. Am J Med 44: 26-38, 1968.	A 482
FOWLER N O: Chronic cor pulmonale. Geriatrics 22/6:156-71, 1967.	A 483
GALY P and PERRIN L-F: Le surfactant alveolaire dans le poumon normal et pathologique. Rev Lyonnaise Med 17: 677-84, 1968.	A 484
GERLACH U: Zur pathogenese der arteriosklerose. Therapiewoche 2: 59-63, 1969.	A 485
GIAMMONA S T, KERNER D and BONDURANT S: Effect of oxygen breathing at atmospheric pressure on pulmonary surfactant. J Appl Physiol 20: 855-8, 1965.	A 486
GROVER R F, ALEXANDER J F and HARTLEY L H: Myocardial function in cor pulmonale. In: Current Research in Chronic Respiratory diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 121-7, 1969.	A 487
HURST J W: Prevention of coronary atherosclerosis. In: The Heart. Arteries and	

List No. 15 Reprint

KILBURN K H, ASMUNDSSON T, BRITT R C and CARDON R: Effects of breathing 10 per cent carbon dioxide on the pulmonary circulation of human subjects. Circulation 39: 639-53, 1969. A 489

LLOYD JR T C: Hypoxic pulmonary vasoconstriction: role of perivascular tissue. J Appl Physiol 25: 560-5, 1968. A 490

MALISZEWSKI T F and BASS D E: 'True' and 'Apparent' thiocyanate in body fluids of smokers and nonsmokers. J Appl Physiol 8: 289-91, 1955. A 491

MASSUMI R A and NUTTER D O: Cardiac arrhythmias associated with Cheyne-Stokes respiration: a note on the possible mechanisms. Dis Chest 54: 21-2, 1968. A 492

McLAUGHLIN R F, TYLER W S and CANADA R O: A study of the subgross pulmonary anatomy in various mammals. Am J Anatomy 108: 149-65, 1961. A 493

MENDENHALL J T: Evaluation and management of pulmonary insufficiency in surgical patients. Surg Clin N Amer 48: 773-8, 1968. A 494

NAEYE R L and LAQUEUR W A: Chronic cor pulmonale. Its pathogenesis in Appalachian bituminous coal workers. Arch Path 90: 487-93, 1970. A 495

OUTHRED K G, McKENZIE H I and WHITE K H: Some findings on the post-mortem association of right ventricular wall thickness and chronic obstructive bronchitis, pneumoconiosis, emphysema and tuberculosis. Med J Aust 2: 950-4, 1970. A 496

PAUTRAT J: Les complications cardiaques des broncho-pneumopathies. G M de France 1: 4993-8, 1967. A 497

PENMAN R W, HOWARD P and STENTIFORD N H: Factors influencing pulmonary gas exchange in patients with acute edematous cor pulmonale due to chronic lung disease. Am J Med 44: 8-15, 1968. A 498

PHILLIPS R W: The electrocardiogram in cor pulmonale secondary to pulmonary emphysema: A study of 18 cases proved by autopsy. Am Heart J 56: 352-71, 1958. A 499

PLATTS M M, HAMMOND J D and STUART-HARRIS C H: A study of cor pulmonale in patients with chronic bronchitis. Q J Med 29: 559-74, 1960. A 500

READ J, LEE J H and PAIN M C: Two groups of subjects with obstructive lung disease, defined by pulmonary vascular reactivity. Public Health Service Publication No. 1787: 229-39, 1968. A 501

SAID S I: Role of pulmonary surfactant in health and disease. Med Clin North Am 51: 391-402, 1967. A 502

SANDERS W L: Heart disease and pneumoconiosis. Thorax 25: 223-5, 1970. A 503

SEKULIC S M, HAMLIN III J T, ELLISON R G and ELLISON L T: Pulmonary surfactant and lung circulation in experimental atelectasis. Am Rev Resp Dis 97: 69-75, 1968. A 504

SHERMAN M: Smoking and heart disease. National Advisory Heart Council : 1-55, 1962. A 505

SHMOCK C L, MITCHELL R S, POMERANTZ B, PRYOR R and MAISEL J C: The electrocardiogram in chronic airways obstruction. The role of bronchitis and emphysema. Chest 60: 335-40, 1971. A 506

STAMLER J: Chronic pulmonary heart disease (Cor pulmonale). In: Lectures on Preventive Cardiology by J Stamler, Grune and Stratton, Inc., New York, A 507

List No. 15 Reprint

STONE R M, GINSBERG R J, COLAPINTO R F and PEARSON F G: Bronchial artery regeneration after radical hilar stripping. Surg Forum 17: 109-10, 1966. A 508

VUGA D: Risposta del tratto bronchiolo-alveolare al fumo di sigaretta. Riflessi sul surfactant e sulla chiarificazione polmonare. Riforma Medica 82: 203-8, 1968. A 509

WEST J B, GLAZIER J B, HUGHES J M and MALONEY J E: Effect of gravity on the morphology of pulmonary capillaries and alveoli. In: Current Research in Chronic Respiratory Diseases. Proceedings of the 11th Aspen Emphysema Conference, Aspen, Colo. U.S. Department of Health, Education, and Welfare, Public Health Service Publication 1879: 135-7, 1969. A 510

AUTHOR INDEX

(Reprint number) followed by pages in the text.

AUERBACH, HAMMOND, GARFINKEL and BENANTE 1972 (28) 19, 18, 17
AUERBACH, HAMMOND, KIRMAN and GARFINKEL 1967 (107) 35, 31
AUERBACH, HAMMOND, KIRMAN and GARFINKEL 1970 (108) 35, 31
AUERBACH, HAMMOND, KIRMAN, GARFINKEL and STOUT 1967 (254) 61, 60
AUERBACH, HAMMOND, KIRMAN, GARFINKEL and STOUT 1968 (109) 35, 31
AUERBACH, STOUT, HAMMOND and GARFINKEL 1961 (173) 44, 43
AUERBACH, STOUT, HAMMOND and GARFINKEL 1962a (174) 44, 43
AUERBACH, STOUT, HAMMOND and GARFINKEL 1962b (175) 44, 43
AUERBACH, STOUT, HAMMOND and GARFINKEL 1963 (29) 19, 16
AUERBACH, STOUT, HAMMOND and GARFINKEL 1964 (905) 187
AUERBACH, STOUT, HAMMOND and GARFINKEL 1966 (30) 19, 16
AUERBACH, STOUT, HAMMOND and GARFINKEL 1968 (176) 44, 43
AVIADO 1972 (623) 128, 127
AVIADO 1969 (110) 35, 32; (624) 128, 127
AVIADO and McKINNEY 1969 (111) 35, 32
AVIADO and PALECEK 1967 (625) 128, 127
AVIADO, SADAVONGVIVAD and CARRILLO 1970 (112) 35, 33; (626) 128, 127
AVIADO and SAMANEK 1965 (627) 128, 127
AVIADO, SAMANEK and FOLLE 1966 (787) 152, 151
AVIADO, WATANABE and BELEJ 1973 (628) 128
AYER and LYNCH 1968 (A 397) 229
AYRES 1968 (1047) 196
AYRES 1970 (A 228) 219
BACHMAN 1970 (1048) 196
BADGER and GREEN 1967 (A 71) 210
BAILEY, HABERMAN and SHEINBERG 1969 (317) 75, 74
BAIR, PORTER, BROWN and WEHNER 1969 (113) 35, 32
BAKER 1970 (A 72) 210
BAKER, OSCHERWITZ, CORLIN, JARBOE, TEISCH and NICHAMAN 1970 (A 338) 225
BALCHUM 1962 (A 229) 219
BALCHUM, BUCKLEY, SHERWIN and GARDNER 1965 (114) 35, 33
BALCHUM, DYBICKI and MENEELY 1960 (A 398) 229
BALCHUM, FELTON, JAMISON, GAINES, CLARKE and OWAN 1963 (389) 93, 92
BALINT, BONDURANT and KYRIAKIDES 1971 (788) 152, 150
BALLENGER 1960 (670) 135, 131
BALLENGER, DAWSON, DeRUYTER and HARDING 1965 (A 458) 234
BALLENGER, McFARLAND, HARDING, KOLL and HALSTEAD 1968 (A 399) 229
BANYAI 1961 (A 73) 210
BANYAI 1962 (A 36) 208
BANYAI 1966 (A 37) 208
BANYAI 1967 (1049) 196
BARACH 1964 (319) 75, 72
BARACH 1966 (A 74) 210
BARACH 1967 (1140) 201
BARACH 1970 (1141) 201
BARACH 1971 (318) 75, 72
BARACH 1967 (A 300) 223
BARACH and SEGAL 1968 (320) 75, 72
BARCLAY 1966 (969) 191
BARCLAY 1969 (A 263) 221
BARCKLEY (1050) 196
BARER, HOWARD and McCURRIE 1967 (A 474) 235
BARNES and SIMPSON 1968 (493) 111, 109
BASS, WHITCOMB and FORMAN 1970 (A 75) 210
BATES 1965 (A 38) 208
BATES 1968 (A 264) 221
BATES 1968 (A 265) 221
BATES 1970 (A 39) 208
BATES 1972 (A 230) 219
BATES, BOUCOT and DORMER 1955 (740) 143, 141
BATES, GORDON, PAUL, PLACE, SNIDAL and WOOLF 1966 (202) 48, 46
BATTISTA and KENSLER 1970a (671) 135, 134
BATTISTA and KENSLER 1970b (672) 135, 134
BAUMANN 1968 (A 40) 208
BAUMBERGER 1927 (A 459) 234
BEAUDRY 1968 (494) 111, 104
BECKERMAN 1967 (841) 184
BECKLAKE, GOLDMAN, BOSMAN and FREED 1957 (115) 35, 33
BEDELL and SEEBOHM 1959 (A 76) 210
BEDELL and SEEBOHM 1966 (60) 28, 24
BEDROSSIAN 1972 (A 188) 217
BEECKMANS 1965 (A 431) 232
BEERENS 1967 (A 231) 219
BEHNKE 1970 (780) 149, 148
BELCHER 1966 (1051) 196
BELL (1142) 201
BELL 1970 (61) 28, 26
BELLOMY (1052) 196
BENNETT 1972 (835) 182, 161
BERARD and EMONOT 1972 (346) 81, 79
BERITIC 1964 (842) 184
BERNDT 1962 (A 339) 225
BERNIER 1957 (A 189) 217
BEST, WALKER, BAKER, DELAQUIS, McGREGOR and McKENZIE 1967 (308) 71, 69
BEUMER 1963 (1053) 196
BICKERMAN and BARACH 1954 (45) 23, 22
BIEGEL and KRUMHOLZ 1968 (241) 57, 56
BIERSTEKER 1968 (495) 111, 106

BIERSTEKER 1969 (496) 111, 106
BIERSTEKER 1969 (497) 111, 106
BISHOP 1963 (A 2) 205
BLACK and HYATT 1971 (A 340) 225
BLACK, HYATT and STUBBS 1972 (62) 28, 26
BLACKBURN, TAYLOR, PARLIN, KIHLBERG and KEYS 1965 (390) 93, 91
BLAIR, HENRY and EHRLICH 1969 (116) 35, 32
BLAKE 1964 (A 77) 210
BLUE 1970 (347) 81, 79
BLUMBERG 1969 (A 190) 217
BLUNDI 1969 (A 191) 217
BOAKE 1958 (242) 57, 56
BOATMAN and MARTIN 1965 (117) 35, 34
BOCHE and QUILLIGEN 1959 (673) 135, 134
BOIN 1969 (1006) 193
BOKHOVEN and NIESSEN 1961 (118) 35, 33
BONDURANT 1960 (789) 152, 150
BONNELL 1955 (119) 35, 34
BONNELL, KAZANTZIS and KING 1959 (120) 36, 34
BONOMO and D'ADDABBO 1964 (217) 51, 50
BONSI (A 192) 217
BOREN 1965 (121) 36, 31
BOREN, BUSET, CORPE, GRZYBOWSKI, NEWMAN, ORGANICK, and LESTER 1966 (A 78) 210
BOREN, DELAHANT and STEENKEN 1965 (122) 36, 33
BOREN, KORY and SYNER 1966 (597) 123, 120
BOREN and KRAHL 1965 (A 475) 235
BORGATTA and EVANS 1968 (2) 11, 8; (970) 191
BOUCOT 1968 (1007) 193
BOUCOT, COOPER and WEISS 1962 (391) 93, 87
BOUDIK, GOLDSMITH, TEICHMAN and KAUFMANN 1970 (498) 111, 108
BOUHUYS, BARBERO, SCHILLING and VAN DE WOESTIJNE 1969a (499) 111, 107
BOUHUYS, GEORG, JÖNSSON, LUNDIN and LINDELL 1960 (A 432) 232
BOUHUYS, JONSSON, LICHTNECKERT, LINDELL, LUNDGREN, LUNDIN and RINGQUIST 1960 (A 433) 232
BOUHUYS and PETERS 1970 (A 400) 229
BOUHUYS, SCHILLING and VAN DE WOESTIJNE 1969b (500) 111, 107
BOUHUYS, WOLFSON, HORNER, BRAIN and ZUSKIN 1969 (392) 93, 90
BOUSHY, KOHEN, BILLIG and HEIMAN 1968 (47) 23, 21
BOUSHY and LEWIS 1964 (46) 23, 21
BOWER 1961 (393) 93, 91
BRILLE 1969 (501) 111, 106
BRILLE 1970 (502) 111, 106
BRILLE, COUDRAY, ISRAEL-ASSELAIN, LE MELLETIER, MICHEL, MIGUÈRES, PHAM and VOISIN 1970 (503) 111, 106
BRINKMAN and BLOCK 1966 (394) 93, 90
BRINKMAN and BLOCK 1968 (203) 48, 47
BRINKMANN and BLOCK 1972 (204) 48, 47
BRINKMAN and BLOCK 1972 (395) 93, 90
BRINKMAN and COATES 1962 (396) 93, 90
BRISCOE and DUBOIS 1958 (A 434) 232
BRITISH MEDICAL JOURNAL 1967 (843) 184
BRITISH MEDICAL JOURNAL 1971 (844) 184
BRITISH MEDICAL JOURNAL 1971 (906) 187
BROCARD 1969 (A 301) 223
BRODINE 1972 (A 232) 219
BROWN 1958 (A 302) 223
BROWN and CAMPBELL 1961 (A 341) 225
BROWNING 1967 (845) 184
CAHAN and KIRMAN 1968 (124) 36, 31
BROWNING and THORP 1969 (1054) 196
BROWNLEE (1143) 201
BRUN, BIOT and KOFMAN 1969 (A 123) 213
BRUN, FOFMAN, GUICHARD and PERRIN-FAYOLLE 1967 (A 14) 206
BRYSIEWICZ, BULUK, CESARZ-FRONCZYK, KORDECKA, LESZCZYŃSKI, ŁUKJAN and SADOKIERSKA 1970 (504) 111, 107
BRYSON and BISCHOFF 1969 (A 193) 217
BUCKLEY and LOOSLI 1969 (123) 36, 33
BUECHNER, BROWN and TRETOLA 1964 (63) 28, 27
BUELL, DUNN and BRESLOW 1967 (321) 75, 73
BULLETIN OF THE LOS ANGELES COUNTY MEDICAL ASSOCIATION 1968 (846) 184
BURCH 1961 (971) 191
BURGER 1968 (A 435) 232
BURGESS (972) 191
BURGESS and BURGESS 1966 (48) 23, 21
BURNS and MAY 1967 (A 342) 225
BURROWS 1962 (64) 28, 25
BURROWS 1966 (A 303) 223
BURROWS 1967 (741) 143
BURROWS 1968 (A 41) 208
BURROWS 1969 (A 304) 223
BURROWS and EARLE 1964 (322) 75, 73
BURROWS and EARLE 1969 (205) 48, 47
BURROWS, FLETCHER, HEARD, JONES and WOOTLIFF 1966 (A 266) 221
BURROWS and KETTEL 1969 (A 267) 221
CAIRD and AKHTAR 1972 (206) 48, 46
CALDWELL and FRY 1969 (A 436) 232
CALIFORNIA GOVERNOR'S ADVISORY COMMITTEE ON CIGARETTE SMOKING AND HEALTH 1964 (1055) 196
CALIFORNIA MEDICAL ASSOCIATION 1967 (1056) 19
CALIFORNIA MEDICAL ASSOCIATION 1968 (A 343) 2
CAMNER and PHILIPSON 1971 (674) 135, 132

CAMNER and PHILIPSON 1972 (675) 135, 132
CAMNER, PHILIPSON and ARVIDSSON 1971 (676) 135, 132
CAMNER, PHILIPSON and ARVIDSSON 1973 (677) 135, 132
CAMNER, PHILIPSON and FRIBERG 1972 (678) 135, 132
CAMPBELL 1969 (A 15) 206
CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE 1966a (309) 71, 69
CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE 1966b (310) 71, 69
CANADIAN DEPARTMENT OF NATIONAL HEALTH AND WELFARE 1966c (311) 71, 69
CANADIAN FAMILY PHYSICIAN 1968 (1057) 196
CANADIAN JOURNAL OF PUBLIC HEALTH 1965 (973) 191
CANADIAN MEDICAL ASSOCIATION JOURNAL 1963 (1008) 193
CANADIAN MEDICAL ASSOCIATION JOURNAL 1964 (974) 191
CANADIAN MEDICAL ASSOCIATION JOURNAL 1967 (975) 191
CANADIAN MEDICAL ASSOCIATION JOURNAL 1969 (1009) 193
CANCER NEWS (976) 191
CANDER and BLUMENTHAL 1963 (65) 28, 25
CANTER and LUCHSINGER 1967 (66) 28, 26
CANTER and LUCHSINGER 1968 (67) 28, 26
CAPLAN, SIMON and REID 1966 (446) 101, 100
CARABASI 1963 (A 79) 210
CARABASI 1966 (A 305) 223
CAREY, DAWSON and MERRETT 1967 (598) 123, 122
CAREY, PHAIR, SHEPHARD and THOMSON 1958 (A 233) 219
CARIELLO (A 42) 208
CARILLI, KOTZEN and FISCHER 1973 (68) 28, 25
CARLSON, DYER and JOHNSON 1968 (125) 36, 34
CARLSON, YOKOYAMA and DICKINSON 1972 (126) 36, 34
CARNOW 1968 (951) 190
CARNOW, LEPPER, SHEKELLE and STAMLER 1969 (A 401) 229
CARSON, GOLDHAMER and CARPENTER 1966 (679) 135, 133
CASARETT 1968 (A 437) 232
CASARETT 1971 (A 234) 219
CASSUTO 1970 (907) 187
CATLETT and KIDERA 1969 (599) 123, 121
CECILIONI 1970 (977) 191
CEDERLÖF 1966 (505) 112, 105
CEDERLÖF 1967 (506) 112, 105
CEDERLÖF, FRIBERG and HRUBEC 1969 (507) 112, 105
CEDERLÖF, FRIBERG, JONSSON and KAIJ 1965 (508) 112, 105
CEDERLÖF, FRIBERG, JONSSON and KAIJ 1966 (509) 112, 105
CELIS, DIAZ, GOROCICA and CANO 1968 (510) 112, 110
CELLERINO and BILLIA 1962 (629) 128, 126
CHADWICK 1967 (1144) 201
CHADWICK 1968 (1058) 196
CHANG 1956 (177) 44, 41
CHANG 1957 (178) 44, 41
CHANG 1958 (179) 44, 41
CHAPMAN and REDISH 1960 (180) 44, 43
CHAPMAN 1965 (742) 143, 142
CHATGIDAKIS 1960 (511) 112, 108
CHERNIACK 1964 (3) 11, 8
CHERNIACK, DOWLING, CARTON, and McBRYDE 1967 (A 344) 225
CHESTER, GILLESPIE and KRAUSE 1969 (A 402) 229
CHIANG and WANG 1970 (630) 128, 126
CHIVERS 1959 (447) 101, 100
CHO, SAMANEK and AVIADO 1968 (631) 128, 127
CHRETIEN 1971 (1062) 197
CHRISTINE 1971 (1010) 193
CHWAT and MORDISH 1971 (512) 112, 109
CIERNIAK, JELONKIEWICZ, SŁODCZYK, CIERNIAK and PAWLAK 1970 (513) 112, 107
CLARK and COCHRANE 1970 (69) 28, 27
CLARKE, GUYATT, ALPERS, FLETCHER and HILL 1970 (632) 128, 126
CLARKE 1972 (397) 93, 90
CLEMENTS 1972 (790) 152, 151
CLOUGH 1956 (1030) 195
CLOUTIER 1967 (A 195) 217
COATES, BOWER and REINSTEIN 1965 (398) 93, 90
COHEN and JENNEY 1962 (A 345) 225
COHEN, HUDSON, CLAUSEN and KNELSON 1972 (231) 54, 53
COHEN 1967 (A 268) 221
COHEN and ROCHESTER 1966 (633) 128, 125
COHEN 1967 (312) 71, 70
COLE and HAMMEL 1961 (A 80) 210
COLLEGE OF GENERAL PRACTITIONERS 1961 (448) 101, 98
COLLEGE HEALTH 1965 (1011) 193
COLLEY and HOLLAND 1967 (449) 101, 98
COLLEY and REID 1970 (450) 101, 99
COLLOQUES INTERNATIONAUX DU CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE 1968 (A 476) 235
COLP, PARK and WILLIAMS 1970 (A 43) 208
COMSTOCK, BROWNLOW, STONE and SARTWELL 1970 (399) 94, 87

EARLE and BURROWS 1972 (A 308) 223
EBERLY, TYLER and GILLESPIE 1966 (127) 36, 34
EBERT 1959 (A 44) 208
EBERT 1961 (A 270) 221
EBERT and PIERCE 1963 (A 3) 205
ECHT 1969 (A 480) 235
ECKARDT 1964 (A 237) 219
ECKARDT 1972 (404) 94, 84
EDELMAN, MITTMAN, NORRIS, COHEN and SHOCK 1966 (601) 123, 121
EDITORIAL 1964 (819) 160, 165
EDWARDS, McKEOWN and WHITFIELD 1959 (451) 101, 98
EDWARDS 1966 (A 159) 215
EDWARDS 1957 (350) 81, 78
EHRLICH and HENRY 1968 (128) 36, 33
EICH, GILBERT and AUCHINCLOSS 1956 (49) 23, 22
EICH, GILBERT and AUCHINCLOSS 1957 (50) 23, 22
EL DIA MEDICO 1967 (853) 184
ELLIOT and TIGHE 1968 (1067) 197
EL-SEWEFY 1970 (522) 113, 109
EL-SEWEFY and AWAD 1971 (523) 113, 109
ELWOOD, PEMBERTON, MERRETT, CAREY and McAULAY 1965 (452) 101, 100
ELY, PEDLEY, HEARNE and STILLE 1970 (405) 94, 87
EMIRGIL, SOBOL, NORMAN, MOSKOWITZ, GOYAL and WADHWANI 1969 (A 86) 211
EMMANUEL, ROSENBLUTH, ANSARI, VILLANO and CARDUCCI 1969 (A 481) 235
ENTERLINE 1967 (A 351) 226
ENTERLINE 1970 (A 406) 229
ENTERLINE and LAINHART 1967 (406) 94, 89
ERIKSSON 1965 (76) 29, 26, 27
ESPINO 1967 (953) 190
EVANG 1964 (854) 184
EVANG 1969 (855) 184
EVANS, WILKES and DALRYMPLE-SMITH 1969 (453) 101, 99
EVERT 1965 (696) 136, 132
FAIN 1971 (A 87) 211
FAIRBAIRN and REID 1958 (232) 54, 52
FALK and BRISCOE 1970 (909) 187
FALK and BRISCOE 1970 (910) 187
FALK, SISKIND and SMITH 1971 (A 124) 213
FALK, TREMER and KOTIN 1959 (697) 136, 133
FALLAT 1970 (77) 29
FALLAT, POWELL, KUEPPERS, NADEL and MURRAY 1971 (79) 29, 26
FALLAT, POWELL, KUEPPERS, LILKER 1973 (78) 29, 26
FARCON and MORALES 1972 (A 309) 223
FEGIZ (A 45) 208
FERIN 1966 (A 441) 232
FERIN 1967 (698) 136
FERIN, URBANKOVA, VICKOVA and REICHRTOVA 1966 (699) 137, 134
FERRIS 1968 (A 238) 219
FERRIS and ANDERSON 1965 (407) 94, 84
FERRIS, ANDERSON and BURGESS 1962 (A 352) 226
FERRIS, BURGESS and WORCESTER 1967 (408) 94, 85
FERRIS, BURGESS and WORCESTER 1968 (409) 94, 86
FERRIS, HIGGINS, HIGGINS, PETERS, VAN GANSE and GOLDMAN 1971 (410) 94, 84
FERRIS, HIGGINS, HIGGINS and PETERS 1973 (411) 94, 84
FERRIS, SPEIZER, WORCESTER and CHEN 1971 (1012) 193
FERRIS and WHITTENBERGER 1966 (A 239) 219
FEUEREISL, KRZHIVANEK, REIL, KUBIK and FELKEL 1972 (524) 113, 108
FIESER 1964 (817) 160, 162
FILLEY 1967 (A 310) 223
FILLEY, BECKWITT, REEVES and MITCHELL 1968 (A 482) 235
FINGERLAND, HUSAK and BENFLOVA 1971 (31) 19, 17
FINKLEA, HASSELBLAD, SANDIFER, HAMMER and LOWRIMORE 1971 (412) 94, 90
FINKLEA, SANDIFER and SMITH 1969 (246) 57, 56
FINLEY 1972 (792) 152
FINLEY and LANDMAN 1972 (793) 152, 151
FISHBEIM 1964 (822) 160, 168
FISHER 1964 (911) 187
FLETCHER 1959 (A 160) 215
FLETCHER 1962 (A 271) 221
FLETCHER 1962 (A 272) 221
FLETCHER 1963 (454) 101, 97
FLETCHER 1963 (A 273) 221
FLETCHER 1965 (A 161) 215
FLETCHER 1965 (A 162) 215
FLETCHER 1967 (A 46) 208
FLETCHER 1967 (A 163) 215
FLETCHER 1968 (207) 48, 47
FLETCHER 1968 (856) 184; (979) 191
FLETCHER 1968 (A 164) 215
FLETCHER 1969 (857) 185
FLETCHER and HORN 1970 (5) 11, 8

FLETCHER, HORN, AS and RAMSTROM 1971 (1068) 197
FLETCHER, HUGH-JONES, McNICOL and PRIDE 1963 (A 311) 223
FLICK and PATON 1959 (602) 123, 120
FLINT, MAXWELL and RENZETTI 1971 (255) 61, 59
FODOR, GLASS and WEINER (1069) 197
FOGARTY 1967 (824) 160, 171
FOGH, FROST and GEORG 1969 (525) 113, 106
FOITZIK, STAEMMLER and POSZICH 1972 (A 197) 217
FOLEY, AMOE, COON and CULVER 1969 (1070) 197
FONTANA (978) 191
FORBES 1967 (A 407) 229
FORD 1971 (1013) 193
FORSTER, ROUGHTON, CANDER, BRISCOE and KREUZER 1957 (744) 143
FOURNIER and ZIVY 1970 (526) 113, 106
FOWLER 1967 (A 483) 235
FRANKLIN and LOWELL 1961 (603) 123, 120, 121
FRANKLIN, MICHELSON, LOWELL and SCHILLER 1958 (A 88) 211
FRANCES, ALESSANDRO, LIPPMANN, PROCTOR and ALBERT 1970 (700) 137, 134
FRASCA, AUERBACH, PARKS and JAMIESON 1968a (256) 61, 60
FRASCA, AUERBACH, PARKS and JAMIESON 1968b (257) 61, 60
FRASCA, AUERBACH, PARKS and JAMIESON 1971 (129) 36, 31
FREDERICKSON 1968 (1071) 197
FREDERICKSON 1970 (1072) 197
FREEMAN 1968 (130) 36, 33
FREEMAN, CRANE, STEPHENS and FURIOSI 1968a (131) 36, 33
FREEMAN, CRANE, STEPHENS and FURIOSI 1968b (132) 36, 33
FREEMAN, CRANE, STEPHENS and FURIOSI 1969 (133) 36, 33
FREEMAN and HAYDON 1964 (134) 36, 33
FREOUR and COUDRAY 1971 (6) 11, 8
FREOUR, COUDRAY, ROUSSEL and SERISE 1966 (527) 113, 106
FRUHMANN 1968 (A 274) 221
FRY 1954 (328) 75, 73
FULLMER 1968 (218) 51, 49
FULLMER, SHORT, ALLEN and WALKER 1969 (219) 51, 50
FURLANETO, ANDERSON and FORAKER 1969 (A 408) 229
FUTORYANSKY, DETSIL, SHUFLAT SIMONCHIK and BARANSKY 1971 (528) 113, 108
GALY and PERRIN 1968 (A 484) 235
GANDEVIA 1969 (529) 113, 109
GANDEVIA and MILNE 1965 (530) 113, 109
GARCIA ECHEVERRIA (858) 185
GARDINER 1963 (A 47) 208
GARFINKEL 1963 (980) 191
GASINSKA and GBUREK 1970 (532) 113, 108
GAUTHIER 1970 (531) 113, 104
GAVRILESCU, TECULESCU, STANESCU and CONSTANTIN 1967 (A 442) 232
GEDDA 1967 (70) 28, 27
GEISER and STEINMANN 1969 (351) 81, 78
GEISLER 1966 (A 165) 215
GEISLER, BACHMANN, LAUMEN, NOLTE WENTZEL and ROST 1972 (80) 29, 27
GERLACH 1969 (A 485) 235
GIAMMONA 1967 (794) 152, 150
GIAMMONA, KERNER and BONDURANT 1965 (A 486) 235
GIAMMONA, TOCCI and WEBB 1971 (795) 152, 150
GILGEN 1970 (7) 11, 8
GILLESPIE and TYLER 1967 (136) 36, 34
GILLESPIE, TYLER and EBERLY 1964 (137) 36, 34
GILLESPIE, TYLER and EBERLY 1966 (138) 37, 34
GLAUSER and GLAUSER 1969 (139) 37, 34
GLAUSER 1971 (A 125) 213
GLUCKMAN 1969 (A 48) 208
GODBER (859) 185
GOFF and GAENSLER 1972 (A 409) 229
GOLDRING, GREENBURG and RATNER 1968 (140) 37, 34
GOLDSMITH 1965 (A 353) 226
GOLDSMITH 1966 (954) 190
GOLDSMITH 1969 (955) 190
GOLDSMITH 1970 (A 240) 219
GOLDSMITH 1971 (912) 187
GOLDSMITH and DEANE 1965 (A 354) 226
GOLDSMITH, GREENBURG, ALTSHULLER, SPICER, CASSELL and LANDSBERG 1966 (A 241) 219
GOLDSMITH, HECHTER, PERKINS and BOHRANI 1962 (413) 94, 92
GOLLI 1970 (533) 113
GONZALES, WEILL, ZISKIND and GEORGE 1968 (A 312) 223
GOTTSCHING and GOTTSCHING 1966 (A355) 226
GOUGH 1955 (A 17) 206
GOUGH 1968 (A 4) 205
GRAY 1959 (141) 37, 33
GREEN and HORN 1968 (1073) 197
GREEN 1968 (247) 57, 55
GREEN 1968a (258) 61, 58
GREEN 1968b (248) 57, 55
GREEN 1968b (259) 61, 58
GREEN 1968c (260) 61, 58

GREEN 1969 (261) 61, 58
GREEN and CAROLIN 1967 (262) 61, 58
GREEN 1965 (410) 229
GREENBERG, MILNE and WATT 1970 (A 356) 226
GREGG 1966 (956) 190
GREGG 1967 (A 357) 226
GRIMLEY 1969 (A 411) 229
GROSS (A 242) 219
GROSS 1964 (81) 29, 25
GROSS 1966 (A 18) 206
GROSS 1967 (701) 137, 131
GROSS 1967 (913) 187
GROSS 1971 (A 412) 230
GROSS and DeTREVILLE 1969 (142) 37, 34
GROSS and DeTREVILLE 1969 (914) 187
GROSS, DeTREVILLE, BABYAK, KASCHAK and TOLKER 1968a (143) 37, 33
GROSS, DeTREVILLE, BABYAK, KASCHAK and TOLKER 1968b (144) 37, 33
GROSS, DeTREVILLE, TOLKER, KASCHAK and BABYAK 1969 (263) 61, 60
GROSS and HATCH 1963 (702) 137, 131
GROVER, ALEXANDER and HARTLEY 1969 (A 487) 235
GSELL 1971 (A 198) 217
GUENTER, WELCH, FERGUSON, HENDERSON and HAMMARSTEN 1971 (A 126) 213
GUENTER, WELCH and HAMMARSTEN 1971 (82) 29, 26
GUENTER, WELCH, RUSSEL, HYDE and HAMMARSTEN 1968 (A 127) 213
GUILLERM, BADRE, SAINDELLE, HEE and FLAVIAN 1968 (1033) 195
GUILLERM, BADRE and VIGNON 1961 (703) 137, 134
GUPTA, PURI, INDIRA and DATTA 1968 (A 358) 226
GUTHRIE (860) 185
GUYATT and ALPERS 1968 (638) 129, 125
GUYATT, BERRY, ALPERS, BRAMLEY and FLETCHER 1970 (639) 129, 125
HAAGEN-SMIT, BRUNELLE and HARA 1959 (145) 37, 33
HACKETT and SUNDERMAN 1968 (A413) 230
HAENSZEL and HOUGEN 1972 (534) 113, 107
HAGERUP and LARSEN 1971 (535) 113 106
HAHN, WESTINGHOUSE, SCHREIBER BRILLMAN, LOMBARD and EISENBERG 1970 (1146) 201
HAIN 1969 (A 166) 215
HALE, OLSEN and MICKEY 1968 (A 443) 232
HALLETT 1965 (A 414) 230
HAMMARSTEN, WELCH, RICHARDSON, PATTERSON and GUENTER 1968 (A 128) 213
HAMMOND (A 199) 217
HAMMOND 1959 (290) 67, 66
HAMMOND 1964 (291) 67, 66
HAMMOND 1964 (861) 185
HAMMOND 1964 (981) 191
HAMMOND 1965 (1074) 197
HAMMOND 1966 (292) 67, 66
HAMMOND 1967 (982) 191
HAMMOND 1967 (A 243) 219
HAMMOND 1968 (A 244) 219
HAMMOND 1968 (A 200) 217
HAMMOND 1969 (A 201) 217
HAMMOND 1971 (983) 191
HAMMOND, AUERBACH, KIRMAN and GARFINKEL 1970 (146) 37, 31
HAMMOND, BERGLUND and KASLOW 1965 (293) 67, 66; (862) 185
HAMMOND, FENT, REED and WILSON 1964 (294) 67, 66
HAMMOND and GERBER 1965 (295) 67, 66
HAMMOND, GRIETHUYSEN, DIBELER SNEDDON and HALLIGAN 1965 (300) 67, 66
HAMMOND and HORN 1958 (296) 67, 66
HAMMOND and LETTON 1965 (297) 67, 66
HAMMOND and STOCKS 1964 (298) 67, 66
HAMMOND and STREET 1964 (299) 67, 66
HAMMOND and WILSON 1965 (301) 67, 66
HANY, BURCKHARDT and BUHLMANN 1967 (536) 113, 106
HARKEN 1968 (829) 160, 176
HARRIS 1963 (A 313) 223
HARRIS, MENEELY, RENXETTI, STEELE and WYATT 1962 (32) 19, 14
HARRISON and REEVES 1968 (A 359) 226
HARTUNG 1968 (A 275) 221
HARTUNG and MEYER-CARLSTADT 1968 (A 167) 215
HARTUNG 1969 (A 276) 221
HARVEY 1969 (1075) 197
HAUSKNECHT 1962 (A 360) 226
HAY 1967 (8) 11, 8
HAYDON, DAVIDSON, LILLINGTON and WASSERMAN 1967 (147) 37
HAYDON, FREEMAN and FURIOSIS 1965 (148) 37, 33
HAYES 1970 (84) 29, 26
HAYES and SUMMERELL 1969 (83) 29, 26
HAYNES, KRSTULOVIC and BELL 1966 (249) 57, 56
HAWAII MEDICAL ASSOCIATION 1968 (1076) 197
HEAD, HEAD, HUDSON and HEAD 1960 (89) 211

HEALY 1971 (A 202) 217
HEATH 1958 (85) 29, 27
HEDRICK 1969 (9) 11, 8
HEDRICK 1971 (1077) 197
HEIMANN 1967 (A 246) 220
HEIMANN 1961 (A 245) 220
HEIMBACH 1971 (233) 54, 52
HEINRICHS and HINS 1968 (A 415) 230
HEISE and MYRVIK 1967 (264) 61, 58
HELMHOLZ 1968 (984) 191
HENION 1971 (A 462) 234
HENRY, EHRLICH and BLAIR 1969 (149) 37, 33
HENRY, FINDLAY, SPANGLER and EHRLICH 1970 (150) 37, 33
HEPPER 1969 (1014) 193
HEPPER, BLACK, DINES and MILLER 1968 (A 314) 223
HEPPER, BRANSCOMB, CHERNIACK PIERCE and MITCHELL 1965(A 91) 211
HEPPER, CARR, ANDERSEN, FONTANA, ROSENOW and HANSON 1970 (1078) 197
HEPPER and HYATT 1964 (A 90) 211
HEPPER, HYATT and FOWLER 1969 (A 416) 230
HEPPLESTON 1970 (A 417) 230
HERBERG 1966 (86) 29, 25
HERNANDEZ, ANDERSON, HOLMES and FORAKER 1966 (151) 37, 31
HERNANDEZ, ANDERSON, HOLMES and FORAKER 1966 (A 19) 206
HERXHEIMER and HOLMSTEDT 1959 (A 361) 226
HERZOG 1969 (A 315) 223
HERZOG, KELLER, MAURER, BAUMANN, and NADJAFI 1968 (A 444) 232
HICKEN, HEATH, BREWER and WHITAKER 1965 (772) 147, 145
HICKEY, SCHOFF and CLELLAND 1967 (329) 75, 73
HIGGINS (985) 191
HIGGINS 1957 (455) 101, 97
HIGGINS 1959 (456) 101, 98
HIGGINS 1966 (A 247) 220
HIGGINS and COCHRAN 1958 (457) 101, 98
HIGGINS, COCHRANE, GILSON and WOOD 1959 (458) 101, 100
HIGGINS, GILSON, FERRIS, WATERS, CAMPBELL and HIGGINS 1968 (459) 102, 100
HIGGINS, GILSON, FERRIS, WATERS, CAMPBELL and HIGGINS 1969 (460) 102, 100
HIGGINS, HIGGINS, LOCKSHIN and CANALE 1968 (414) 94, 88
HIGGINS and OLDHAM 1962 (461) 102, 100
HIGGINS, OLDHAM, COCHRANE and GILSON 1956 (462) 102, 97
HIGGINS and KJELSBERG 1967 (415) 95, 90
HILDING 1956a (704) 137, 134
HILDING 1956b (705) 137, 134
HILDING 1967 (706) 137
HILDING and FILIPI 1966 (707) 137, 134
HILL 1928 (708) 137, 134
HISLOP 1964(1079) 197
HOFFMAN 1967 (863) 185
HOGG, MACKLEM and THURLBECK 1972 (A 316) 224
HOLCOMB and MEIGS 1972 (416), 95, 86
HOLDAWAY and TURK 1967 (A 362) 226
HOLE and WASSERMAN 1965 (A 129) 213
HOLLAND, MILIC-EMILI, MACKLEM and BATES 1968 (745) 143
HOLLAND 1963 (A 363) 226
HOLLAND 1968 (A 277) 221
HOLLAND and ELLIOTT 1968 (463) 102, 99
HOLLAND, HALIL, BENNETT and ELLIOTT 1969a (464) 102, 99
HOLLAND, HALIL, BENNETT and ELLIOTT 1969b (465) 102, 99
HOLLAND, HALIL and ELLIOTT 1969c (466) 102, 99
HOLLAND, KOZLOWSKI and BOOKER 1963 (265) 61, 58
HOLLAND and REID 1965 (467) 102, 98
HOLLAND, REID, SELTSER and STONE 1965 (468) 102, 97
HOLLAND and STONE 1965 (417) 95, 87
HOLLAND, WILSON, MORRIS, McCALL and LANZ 1958 (266) 61, 58
HOLMA 1969 (709) 137, 132
HONG, GANDEVIA and LOVELL 1967 (537) 114, 109
HORAK 1969 (10) 11, 8
HORN 1966 (1015) 193
HORN and WAINGROW 1966 (A 364) 226
HOROWITZ 1969 (352) 81, 79
HORTON, TYE and STEMMER 1963 (A 418) 230
HORTON 1965 (1016) 193
HOWARD 1970 (469) 102, 99
HUHTI 1965 (538) 114, 105
HUHTI 1966 (539) 114, 105
HUHTI 1967 (604) 123, 120
HUHTI, RYHANEN, VUOPALA and TAKKUNEN 1970 (540) 114, 105
HUKILL 1963 (1147) 201
HUNT 1968 (A 278) 221
HURST 1959 (A 130) 213
HURST (A 488) 235
HUTCHISON, COOK, BARTER, HARRIS and HUGH-JONES 1971 (88) 29, 26
HUTCHISON, BARTER, COOK, LAWS MARTELLI and HUGH-JONES, 1972 (87) 29, 26
HUTCHISON 1968 (830) 160, 177

HUTTEMANN, OSWALD, LODE and HUCKAUF 1971 (640) 129, 125
HUTTEMANN, OSWALD, LODE and HUCKAUF 1972 (641) 129, 125
HUTTNER and HUTTNER (A 317) 224
HYATT (986) 192
HYATT (A 203) 217
HYATT, KISTIN and MAHAN 1964 (418) 95, 88
HYATT and WILCOX 1961 (A 445) 232
HYDE and HYDE 1956 (A 49) 208
IDE, SUNTZEEF and COWDRY 1959 (183) 44, 42
INGRAHAM (A 248) 220
INOH and AVIADO 1971 (152) 37, 32
INTERNATIONAL SYMPOSIUM IN SAN JUAN 1971 (541) 114, 105
IRNELL and KIVILOOG 1968 (542) 114, 105
ISHIKAWA, BOWDEN, FISHER and WYATT 1969 (33) 19, 17
ISHIKAWA, FATTAL, ZYLAK, CHERNIACK and WYATT 1968 (A 5) 205
ITO and AVIADO 1968a (153) 37, 33; (642) 129, 127
ITO and AVIADO 1968b (154) 37, 32
IZARD 1967 (A 463) 234
JACKSON and BERNARD 1968 (A 92) 211
JACOBS 1970 (834) 161, 181
JAMES 1963 (1080) 197
JAMES 1965 (A 365) 226
JAMES and ROSENTHAL 1961 (302) 68
JAMES 1970 (643) 129, 126
JANCIK 1970 (543) 114, 106
JANCIK and JANCIK-MAK 1972 (544) 114, 108
JARVINEN 1960 (1081) 197
JARVINEN, PATIALA and THOMANDER 1966 (545) 114, 105
JELEA, ILIE and GAVRILA 1964 (546) 114, 108
JERRY and RITCHIE 1964 (A 20) 206
JIMINEZ-DIAZ and CUENZE 1935 (353) 81, 79
JOANNIDES 1965 (A 93) 211
JOHANNSEN and PREIBISZ 1966 (644) 129, 126
JOHNSTON and HARRIS 1965 (A 94) 211
JOHNSTON and KAUFFMAN 1970 (A 50) 208
JONES 1970 (1082) 198
JONES and THOMAS 1971 (89) 29, 26
JONES, BURROWS and FLETCHER 1967 (208) 48, 47
JONES, JONES and EDWARDS 1971 (A 95) 211
JONES, BAETJER and REID 1971 (267) 61, 59
JONES, BOLDUC and REID 1972 (268) 61, 59
JONGKEES 1965 (987) 192
JORGENSEN and SVENSSON 1970 (547) 114, 105
JOULES 1954 (1017) 193
JOURNAL OF THE AIR POLLUTION CONTROL 1966 (915) 188
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1965 (916) 188
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1965 (957) 190
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1966 (917) 188
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1967 (918) 188
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1969 (919) 188
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1969 (988) 192
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION 1972 (1083) 198
JOURNAL OF IOWA MEDICAL SOCIETY 1968 (864) 185
JOURNAL OF IOWA MEDICAL SOCIETY 1969 (1018) 193
JOURNAL OF THE MISSISSIPPI STATE MEDICAL ASSOCIATION (1084) 198
JOURNAL OF THE NATIONAL MEDICAL ASSOCIATION 1967 (1019) 193
JULICH and RUCKER 1969 (A 51) 208
KAATZSCH 1969 (A 168) 215
KAHN 1966 (303) 68, 65
KAHANA, ARONOVITCH and PLACE 1963 (51) 23, 21
KALACIC 1970 (548) 114, 108
KAMINSKI, FANCHER and CALANDRA 1968 (710) 137, 133
KAMPMEIER 1964 (818) 160, 164
KARPICK, PRATT, ASMUNDSSON and KILBURN 1970 (184) 44, 43
KATZ and KUNOFSKY 1964 (354) 81, 78
KELSEY, MOOD and ACHESON 1968 (419) 95, 86
KENDIG 1967 (A 366) 226
KENNEDY and ELLIOTT 1970 (712) 137, 134
KENSLER 1967 (711) 137, 133
KENSLER and BATTISTA 1963 (713) 137, 133
KENSLER and BATTISTA 1966 (714) 137, 133
KHOSLA, MEHROTRA and ANKLESARIA 1969 (781) 149, 148
KIBELSTIS 1972 (420) 95, 88
KILBURN 1967 (A 96) 211
KILBURN 1967 (715) 137, 131
KILBURN 1968 (716) 137, 131
KILBURN, ASMUNDSSON, BRITT and CARDON 1969 (A 489) 236
KILPATRICK 1971 (A 97) 211
KINSELLA 1962 (A 279) 222
KIRSCHENFELD 1963 (A 98) 211
KISS 1966 (605) 123, 121
KLEIN 1970 (A 6) 205

KLEIN 1970 (989) 192
KLEIN, SALVAGGIO and KUNDUR 1969 (A 367) 226
KLEINFELD, MESSITE, SWENCICKI and SHAPIRO 1968 (421) 95, 87
KLER 1945 (250) 57, 55
KLIDE and AVLADO 1968 (645) 129, 127
KNYVETT 1967 (355) 81, 80
KOLLER 1968 (865) 185
KORDICK, BULBRING and BURN 1952 (717) 138, 137
KOTIN 1964 (A 249) 220
KOTIN 1967 (1148) 201
KOTIN 1970 (1149) 201
KOURILSKY, BRILLE and HATTE 1966 (549) 114, 106
KOURILSKY, HAPPERT and FREDY 1966 (A 204) 217
KOWALYSHYN and SATALINE 1969 (A 131) 213
KRAHL and BULMASH 1969 (718) 138, 134
KREYBERG 1969 (A 205) 218
KROEKER and LEON 1962 (356) 81, 80
KRUEGER and SMITH 1958 (719) 138, 132
KRUMHOLZ 1969 (A 318) 224
KRUMHOLZ, CHEVALIER and ROSS 1964 (746) 143, 141
KRUMHOLZ, CHEVALIER and ROSS 1965 (747) 143, 141
KRUMHOLZ, CHEVALIER and ROSS 1965 (773) 147, 145
KRUMHOLZ and HENDRICK 1973 (422) 95, 91
KUCEWICZ 1969a (550) 114, 107
KUCEWICZ 1969b (551) 114, 107
KUEPPERS 1969 (A 132) 213
KUEPPERS 1971 (A 133) 213
KUEPPERS 1971 (A 134) 213
KUEPPERS, FALLAT and LARSON 1969 (A 135) 213
KUPKA and GOLDSMITH 1962 (A 368) 226
KYLE and RIESEN 1970 (269) 62, 59

LABELLE, BEVILACQUA and MUEGER 1966 (720) 138, 132
LABELLE, LONG and CHRISTOFANO 1955 (A 446) 232
LAENNEC 1819 (34) 19, 14
LAKE 1969 (552) 115, 109
LAMB and REID 1969 (270) 62, 59
LAMBERT and REID 1970 (470) 102, 99
LANCASTER and TOMASHEFSKI 1963 (357) 81, 78
LANDAU and MORTON 1961 (990) 192
LANGER and FISHER 1956 (A 447) 233
LANGSTON 1972 (A 206) 218
LAPP, HANKINSON, BURGESS and O'BRIEN 1972 (423) 95, 89
LA PRESSE MEDICALE 1970 (958) 190
LARSEN 1970 (A 280) 222
LARSON 1963 (606) 123, 121
LARSON 1965 (35) 19, 14
LARSON 1966 (920) 188
LARSON and BARMAN 1965 (A 136) 213
LARSON, BARMAN, KUEPPERS and FUDENBERG 1970 (90) 29, 27
LARSON, FUKUDA and MURRAY 1964 (A 464) 234; 1965 (774) 147, 145
LAURELL 1971 (921) 188
LAURENZI, GUARNERI, ENDRIGA and CAREY 1963 (271) 62, 60
LAWS and HEARD 1962 (A 53) 208
LAWTHER 1966 (358) 81, 78
LEBOVITZ, LEBOVITZ and SILVERMAN 1969 (A 99) 211
LEBRUN-BRAIS, BLANCHETTE and PROVOST 1971 (A 137) 213
LECKERT 1964 (A 52) 208
LEFCOE and WONNACOTT 1970 (553) 115, 104
LEGRAND, BOTTO and LESOBRE 1971 (359) 81, 79
LEIBESCHUETZ 1959 (471) 102, 97
LEMLE, VIEIRA, MILWARD and MIRANDA 1970 (A 369) 227
LEMON and WALDEN 1966 (330) 75, 74
LEPINE and MYRE 1969 (52) 23, 21
LEUCHTENBERGER and LEUCHTENBERGER 1965 (272) 62, 60
LEUCHTENBERGER and LEUCHTENBERGER 1970 (A 207) 218
LEUCHTENBERGER, LEUCHTENBERGER and DOOLIN 1958 (273) 62, 60
LEUCHTENBERGER, LEUCHTENBERGER, ZEBRUN and SHAFFER 1960 (274) 62, 60
LEVIN (1150) 201
LEVINE, BIGELOW, HAMSTRA, BECKWITT, MITCHELL, NETT, STEPHEN and PETTY 1967 (A 100) 211
LEVINE, TALAMO, SHANNON and KAZEMI 1970 (91) 29, 26
LEWIS and NICHOLLS 1972 (797) 152, 151
LEWIS and KERBY 1965 (A 419) 230
LEWIS, LAPP and BURRELL 1970 (251) 57, 56
LEWIS, LYLE and MILLER 1969 (796) 152, 151
LICKINT 1956 (A 169) 215
LIEBERMAN 1969 (A 138) 214
LIEBERMAN, MITTMAN and SCHNEIDER 1969 (A 139) 214
LIEBOW 1959 (775) 147, 145
LINDALL 1970 (A 250) 220
LINDALL, MEDINA and GREIMER 1967 (92) 29, 24
LISTER 1971 (866) 185
LLOYD 1968 (A 490) 236
LOB 1970 (A 420) 230
LONG 1964 (1085) 198
LOOSLI 1968 (A 170) 215
LOPEZ-MAJANO, KIEFFER, MARINE, GARCIA and WAGNER 1969 (A 101) 211
LORD, GAZIOGLU and KALTREIDER 1969 (A 319) 224
LOUDON 1969 (A 448) 233
LOUDON and SHAW 1967 (A 449) 233
LOURENCE, KLIMER and BOROWSKI 1971 (721) 138, 132
LORENZONI 1967 (1020) 193
LOWE 1956 (360) 82, 78
LOWE 1968 (A 171) 215
LOWE, CAMPBELL and KHOSLA 1970 (472) 102, 100
LOWE and KHOSLA 1972 (473) 102, 100
LOWE, PELMEAR, CAMPBELL, HITCHENS, KHOSLA and KING 1968 (474) 102, 100
LOWELL 1959 (361) 82, 79
LOWELL, FRANKLIN, MICHELSON and SCHILLER 1956 (362) 82, 80
LOWRY and SCHUMAN 1956 (155) 38, 33
LUBAN-PLOZZA 1967 (1086) 198
LUDWIG and PYLE 1969 (1087) 198
LUNDAR 1965 (867) 185
LUNDMAN 1966 (554) 115, 105
LUPU and VELICAN 1962 (798) 152, 151
LUPU, VELICAN and RACOVEANU 1966 (363) 82, 79
L'UNION MEDICALE DU CANADA 1968 (991) 192
LYNCH (1088) 198
LYONS 1965 (A 54) 208
LYONS, RYDER, CAMPBELL and GOUGH 1972 (475) 102, 100

MILLER and SPROULE 1966 (648) 129
MILLER 1964 (1096) 198
MILLER 1967 (A 103) 212
MILLS 1950 (304) 68
MILLS and BAISCH 1965 (A 375) 227
MILNE and WILLIAMSON 1972A (477) 102, 99
MILNE and WILLIAMSON 1972B (478) 102, 99
MITCHELL 1962 (A 453) 233
MITCHELL 1962 (53) 23, 21
MITCHELL 1964 (A 283) 222
MITCHELL 1966 (960) 190
MITCHELL 1969 (998) 192
MITCHELL, MAISEL, DART and SILVERS 1971 (1024) 193
MITCHELL, RYAN, PETTY and FILLEY 1966 (186) 44, 41
MITCHELL, SILVERS, DART, PETTY, VINCENT, RYAN and FILLEY 1968 (A 284) 222
MITCHELL, TOLL and FILLEY 1962 (A 7) 205
MITCHELL, VINCENT and FILLEY 1964 (54) 23, 21
MITCHELL, WALKER and MAISEL 1968 (782) 149, 148
MITCHELL, WALKER, SILVERS, DART and MAISEL 1969 (A 21) 206
MITCHELL, WEBB and FILLEY 1964 (332) 75, 73
MITTMAN 1967 (A 104) 212
MITTMAN 1972 (159) 38, 31
MITTMAN 1972 (A 141) 214
MITTMAN, LIEBERMAN, MARASSO and MIRANDA 1971A (94) 30, 26
MITTMAN, LIEBERMAN, MARASSO and MIRANDA 1971B (95) 30, 26
MOERSCH 1968 (1097) 198
MOFFAT and SUTHERLAND 1967 (A 376) 227
MOHANTY and GUPTA 1968 (608) 123, 121
MOLHO, RAZ and KREISLER (A 321) 224
MOLYNEUK and TOMBLESON 1970 (479) 103, 100
MONSON 1970 (A 377) 227
MOOLTEN 1968 (723) 138
MOORE and VINCENT (1098) 198
MORGAN 1971 (801) 152, 151
MORGAN 1972 (A 210) 218
MORGAN 1968 (1099) 198
MORGAN 1967 (A 174) 215
MORGAN 1968 (A 285) 222
MORGAN 1971 (A 421) 230
MORIYAMA 1963 (1025) 194
MORIYAMA, DAWBER and KANNEL 1966 (1026) 194
MORK 1962 (366) 82, 78
MORTON 1969 (750) 143, 142
MORTON 1944 (751) 143, 142
MORTON and TURNBULL 1968 (A 322) 224
MOTLEY 1960 (A 57) 209
MOTLEY 1971 (235) 54, 52
MOTLEY and KUZMAN 1958 (752) 143, 141
MOTLEY and PHELPS 1964 (A 251) 220
MOTLEY and YANDA 1966 (236) 54, 53
MUELLER 1969 (1100) 198
MUELLER, KEBLE, PLUMMER and WALKER 1971A (425) 95, 91
MUELLER, WALKER and PLUMMER 1971B (426) 95, 91
MULDOON and WARWICK 1972 (480) 103, 100
MULLER 1959 (A 286) 222
MURPHY, KATZ, MASSARO and LUCHSINGER 1962 (96) 30, 25
MURPHY, FERRIS, BURGESS, WORCESTER and GAENSLER 1971 (A 422) 230
MURPHY, LENG, ULRICH and DAVIS 1963 (A 423) 230
MURRAY 1967 (879) 186
MYDLIL and TOMANEK 1964 (1101) 198
MYRVIK and EVANS 1967 (275) 62, 58
NADEL and COMROE 1961 (649) 129, 126
NADEL, SALEM, TAMPLIN and TOKIWA 1965 (A 454) 233
NAEYE 1972 (427) 95
NAEYE and DELLINGER 1972 (A 424) 230
NAEYE and LAQUEUR 1970 (A 495) 236
NAEYE, MAHON and DELLINGER 1971 (428) 95, 88
NAKASHIMA 1938 (724) 138, 133
NAKAJIMA 1966 (367) 82, 78
NANDI, HERSHEL, SLONE, SHAPIRO and LEWIS 1969 (160) 38, 34
NASIELL 1968 (222) 51, 49
NEBRASKA STATE MEDICAL JOURNAL 1968 (931) 188
NEGREIROS 1968 (A 175) 215
NERI, MANDEL, O'CONNOR and LARSON 1970 (559) 115, 104
NEW ENGLAND MEDICAL JOURNAL 1963 (1153) 201
NEWMAN, VATTER and REISS 1967 (A 22) 206
NICOLAS 1964 (223) 51, 50
NICKLAUS, STOWELL, CHRISTIANSEN and RENZETTI 1966 (A 58) 209
NIDEN 1969 (A 425) 230
NIESENBAUM 1968 (97) 30, 25
NIEWOEHNER, KLEINERMAN and KNOKE 1972 (212) 48, 47
NISHIMOTO, BURROWS, MIYANISHI, KATSUTA, SHIGENOBU and KETTEL 1970 (560) 115, 109
NOMIYAMA, NOMIYAMA and MATSUI 1971 (A 142) 214
NORMAN-TAYLOR and DICKINSON 1972 (481) 103, 99
NTRDA BULLETIN (1035) 195
NYLAN 1968 (831) 160, 178

OCHSNER (1103) 199
OCHSNER (880) 186
OCHSNER (1104) 199
OCHSNER 1967 (A 252) 220
OCHSNER 1968 (832) 160, 179
OCHSNER 1968 (1102) 199
OCHSNER 1971 (961) 190
OCHSNER and DAMRAU 1970 (A98) 30, 27
OLSEN, FONTANA, PEABODY and ORDSTRAND 1968 (1036) 195
OLSEN and GILSON 1960 (482) 103, 97
ORR 1969 (1105) 199
OSWALD 1964 (A 105) 212
OSWALD 1964 (A 287) 222
OSWALD 1967 (A 106) 212
OSWALD 1968 (932) 188
OSWALD, HAROLD and MARTIN 1953 (483) 103, 97
OSWALD and MEDVEI 1955 (484) 103, 97
OTTO 1969 (A 23) 206
OTTO and HINUBER 1972 (A 378) 227
OTTO, ZEILHOFER and REISSINGER 1970 (37) 19, 17
OUTHRED and FLYNN 1960 (561) 115, 109
OUTHRED, McKENZIE and WHITE 1970 (A 496) 236
OVERHOLT 1961 (A 211) 218
OVERHOLT 1964 (1154) 201
OVERHOLT 1967 (A 212) 218
OVERHOLT, OLIYNYK and CADY (A213) 218
OWSINSKI, JANUS and MYSIK 1971 (562) 115, 107
OYANGUREN, DONOSO, PRIETO, VARGAS and PAZ 1972 115, 110
PAGE 1967 (1106) 199
PAIN, GLAZIER, SIMON and WEST 1967 (753) 144, 142
PALECEK and AVIADO 1967 (650) 129, 127
PALECEK, OSKOUI and AVIADO 1967 (651) 130, 127
PALECEK, PALECEKOVA and AVIADO 1967 (161) 38, 32
PALMER (1107) 199
PALMER and DIAMENT 1970 (A 379) 227
PANZER 1972 (38) 19
PANZER 1972 (933) 188
PARADE 1969 (783) 149, 148
PARAS, MERCADO and QUINTERO 1970 (564) 115, 110
PARAS, MERCADO and QUINTERO 1971 (565) 115, 110
PARNELL, ANDERSON and KINNIS 1966 (252) 57, 56
PASQUAZZIM 1968 (A 107) 212
PATTLE 1958 (276) 62, 53
PATTLE 1965 (277) 62, 58
PATTLE and BURGESS 1957 (A 426) 230
PAUL 1968 (934) 188
PAUTRAT 1967 (A 497) 236
PAVIA, SHORT and THOMSON 1970 (725) 138, 131
PAVIA, THOMSON and POCOCK 1971 (726) 138, 131
PAVLIK and CERMAKOVA 1964 (368) 82, 79
PAYNE and KJELSBERG 1964 (429) 95, 90
PEABODY 1962 (1108) 199
PELZER and THOMSON 1966 (652) 130, 125
PEMBERTON 1966 (1027) 194
PEMBERTON 1968 (A 176) 215
PEMBERTON and GOLDBERG 1954 (333) 75, 73
PENMAN 1969 (754) 144
PENMAN 1970 (A 427) 230
PENMAN and ASTIN 1968 (A 323) 224
PENMAN and HOWARD 1966 (755) 144, 142
PENMAN, HOWARD and STENTIFORD 1968 (A 498) 236
PENMAN, O'NEILL and BEGLEY 1970 (A 324) 224
PENNSYLVANIA HEALTH 1965 (1109) 199
PENNSYLVANIA MEDICINE 1969 (1110) 199
PERALES 1971 (A 380) 227
PETERS and MILLERS 1960 (609) 123, 122
PETERS and PRICKMAN 1957 (935) 188
PETERS and FERRIS 1967 (430) 95, 85
PETERS and FERRIS 1967 (431) 95, 85
PETERSON, LONGERGAN and HARDINGE 1968, (610) 123, 122
PETROVA 1956 (566) 115, 108
PETTY (1111) 199
PETTY 1970 (A 108) 212
PETTY, BRINK, MILLER and CORSELLO 1970 (611) 123, 122
PETTY and NETT 1969 (A 109) 212
PETTY, RYAN and MITCHELL 1967 (39) 19, 17
PHELPS and KOIKE 1962 (237) 54, 53
PHILLIPS 1964 (881) 186
PHILLIPS, PHILLIPS and THOMPSON 1956 (A 177) 215
PHILLIPS 1966 (A 382) 227
PHILLIPS 1958 (A 499) 236
PHYSICAL THERAPY 1967 (936) 188
PHYSICAL THERAPY 1968 (937) 189
PICK 1960 (1112) 199
PIERCE 1968 (A 325) 224
PIPER 1958 (756) 144
PIRCHER 1972 (A 326) 224
PISTAWKA 1969 (A 327) 224
PLATT and BOINES 1965 (1113) 199
PLATTS, HAMMOND and STUART-HARRIS 1960 (A 500) 236
POCHMON, SKARABELLOVA and LEGOSTOV 1968 (567) 115, 108

ROSENBLATT 1970 (338) 76, 72
ROSENBLATT 1972 (339) 76, 72
ROSENBLUM 1964 (886) 186
ROSENKRANTZ, ESBER and SPRAGUE 1969 (803) 153
ROSENKRANTZ and SPRAGUE 1969 (A 466) 234
ROSS 1968 (A 218) 218
ROSS, McMICHAEL, EADIE, LEES, MURRAY and PINKERTON 1966 (A 181) 216
ROSS, LEY, KRUMHOLZ and RAHBARI 1967 (759) 144, 141
ROWE and ROWE 1965 (372) 82, 79
ROWLANDS, CADENA and GROSS 1967 (804) 153, 151
ROYAL COLLEGE OF PHYSICIANS 1962 (11) 11, 8
ROYAL COLLEGE OF PHYSICIANS 1971 (12) 11, 8
ROYAL SOCIETY OF HEALTH JOURNAL 1971 (887) 186
RUFF, SALEM, BUSY, de VARNEJOUL, EVEN and BROUET 1972 (655) 130, 125
RUIKKA, SOURANDER and KASANEN 1966 (573) 116, 105
RULLIERE and SAIGOT 1971 (13) 11
RYAN, McDONALD and DEVINE 1955 (190) 45, 43
RYAN 1968 (1119) 199
RYDER 1966 (1002) 192
RYDER, LYONS, CAMPBELL and GOUGH 1970 (489) 103, 100
RYDER, DUNNILL and ANDERSON 1971 (191) 45, 42
RYDER, THURLBECK and GOUGH 1969 (A 28) 207
RYLANDER 1968 (279) 62, 59
RYLANDER 1969 (253) 57, 55
RYLANDER 1969 (280) 62, 59
RYLANDER 1970 (14) 11, 8
RYLANDER 1971 (281) 62, 59
SACHS 1972 (805) 153, 151
SACHS and FINLEY 1972 (1039) 195
SACHS 1970 (942) 189
SADOUL 1968 (A 29) 207
SADOUL, LAZENAIRE, LAMBERT and BERNADAC 1970 (A 62) 209
SAFFIOTTI, BORG, GROTE and KARP 1964 (A 455) 233
SAHA and JAIN 1970 (56) 23, 21
SAID 1967 (A 502) 236
SAINDELLE, RUFF, GUILLERM and PARROT 1968 (806) 153
SALATA 1966 (A 255) 220
SAMANEK and AVIADO 1965 (656) 130, 127
SAMANEK and AVIADO 1966 (777) 147, 145
SAMANEK, AVIADO and PESKIN 1965 (657) 130, 127
SANDERS 1970 (A 503) 236
SANDERUD 1958 (192) 45, 42
SANGHVI and KOTIA 1963 (785) 149, 148
SANO, YODOYAMA and RHOADS 1972 (100) 30, 27
SARIC and GOLDSMITH 1964 (A 428) 230
SAUNDERS 1958 (A 467) 234
SCADDING 1966 (A 112) 212
SCADDING 1969 (A 63) 209
SCHARBORT 1967 (729) 138, 133
SCHLEUSENER, TALAMO, PARE and THURLBECK 1968 (A 145) 214
SCHLOTZHAUER and SCHMELTZ 1967 (A 468) 234
SCHMIDT 1962 (A 182) 216
SCHMIDT 1968 (A 183) 216
SCHOETTLIN 1962 (238) 54, 52
SCHUMAN 1966 (A 383) 227
SCHUMAN 1968 (833) 161, 180
SCHUMAN 1970 (1156) 202
SCHUMAN 1971 (613) 124
SCHUNEMANN 1970 (A 384) 227
SCHWABER 1968 (A 113) 212
SCIENCE NEWS LETTER 1964 (1029) 194
SCIENCE NEWS 1966 (943) 189
SCIENCE NEWS 1967 (1120) 199
SCOTT and WALKER 1965 (888) 186
SEEBOHM and BEDELL 1963 (57) 23, 21
SEELY, ZUSKIN and BOUHUYS 1971 (614) 124, 122
SEGAL and DULFANO 1965 (373) 82, 79
SEKULIC, HAMLIN, ELLISON and ELLISON 1968 (A 504) 236
SEKULIC, SAMLIN, ELLISON and ELLISON 1968 (807) 153, 150
SEPPILLI (1121) 199
SEVCIK 1967 (658) 130, 125
SHAH, WARAWADEKAR, DESHMUKH and PHUTANE 1959 (374) 82, 78
SHAMBAUGH 1967 (825) 160, 172
SHARP, PAUL, LEPPER, McKEAN and SAXTON 1965 (436) 96, 91
SHERMAN 1962 (A 505) 236
SHITO, HAMADA, YASUTARO, EMURA, MITANI, MATSUDA, INOUE, SAWAL, KAWAMURA and OKUBO 1967 (213) 48, 47
SHMOCK, MITCHELL, POMERANTZ, PRYOR and MAISEL 1971 (A 506) 236
SHORE and AVIADO 1969 (659) 130, 127
SHORT, JOHNSON and LEY 1939 (437) 96, 87
SHUBIN 1966 (1040) 195
SIDEL 1967 (1122) 199
SIEDLECKI 1970 (944) 189
SIERING (A 328) 224
SILEN, BROWN and EISEMAN 1959 (A 385) 227
SIMON 1964 (A 64) 209
SIMON 1966 (1157) 202
SIMONSSON 1962 (660) 130, 126
SIMONSSON 1965 (661) 130, 126
SIMONSSON 1965 (214) 48, 46
SIMONNSON, JOCOBS and NADEL 1967 (A 456) 233

SIMPSON 1968 (215) 48, 46
SIMPSON 1968 (A 65) 209
SIRTORI (1123) 199
SLUIS-CREMER and SICHEL 1968 (574) 116, 108
SLUIS-CREMER, WALTERS and SICHEL 1967b (576) 116, 108
SLUIS-CREMER, WALTERS and SICHEL 1967a (575) 116, 108
SMITH, FALK and SISKIND 1971 (A 146) 214
SMITH, SMITH and McCALL 1960 (165) 38, 34
SNIDER 1968 (A 114) 212
SNIDER, DOCTOR, DEMAS and SHAW 1971 (375) 82, 78
SOBONYA and KLEINERMAN 1972 (193) 45, 42
SPAIN 1963 (A 219) 218
SPAIN 1969 (194) 45, 42
SPAIN, BRADESS, TARTER and MATERO 1970 (195) 45, 42
SPEAR, DAUGHTRY, CHESNEY and MARKS 1961 (A 115) 212
SPICER 1964 (A 256) 220
SPIEGEL and COHEN 1970 (1124) 199
SPODINK, CHUSHMAN, KERR, BLIDE and SPICER 1966 (239) 54, 52
SPOTNITZ 1966 (A 257) 220
SPURGASH, EHRLICH and PETZOLD 1968 (282) 62, 60
STAMLER (A 507) 236
STANEK, FODOR, HEJL, WIDIMSKY, CHARVAT, SANTRUCEK, ZAJIC and VAVRIK 1966 (577) 116, 108
STANESCU, GAVRILESCU and TECULESCU 1968 (615) 124, 120
STANESCU, PILAT, GAVRILESCU, TECULESCU and CRISTESCU 1967 (578) 116, 108
STANESCU, TECULESCU, PACURARU and GAVRILESCU 1968 (760) 144, 141
STASZEWSKI 1960 (A 220) 218
STEBBINGS 1971A (438) 96, 89
STEBBINGS 1971B (439) 96, 89
STEBBINGS 1971C (440) 96, 89
STEBBINGS 1971D (441) 96, 89
STEBBINGS 1972 (A 386) 227
STEBBINGS 1973 (A 387) 228
STEDMAN and MILLER 1967 (A 469) 234
STEINFELD 1972 (1158) 202
STEPHENS, FREEMAN and EVANS 1971 (166) 38, 33
STERLING 1967 (662) 130, 126
STEVENS, HNILICA, JOHNSON, BELL 1971 (101) 30, 26
STEVEN 1971 (A 147) 214
STEWART 1970 (A 388) 228
STEWART 1967 (1125) 200
STOKINGER, WAGNER and DOBROGORSKI 1957 (A 429) 230
STONE, GINSBERG, COLAPINTO and PEARSON 1966 (A 508) 237
STORY 1964 (A 116) 212
STRAWBRIDGE 1960A (167) 38, 31
STRAWBRIDGE 1960B (168) 38, 34
STRAWBRIDGE 1960C (169) 38, 34
STREIT (1126) 200
STRESEMANN 1969 (A 258) 220
STRIEDER and KAZEMI 1967 (761) 144, 142
STRIEDER, MURPHY and KAZEMI 1968 (762) 144, 142
STROBEL and GSELL 1965 (579) 116, 107
STRONG, RICHARDS, MCGILL, EGGEN and MCMURRY 1969 (786) 149, 148
STUART-HARRIS 1968 (763) 144
STUART-HARRIS 1971 (A 184) 216
STURGIS 1967 (962) 190
STURGIS 1971 (963) 190
STUBER 1967 (1127) 200
SUFRIN 1970 (A 329) 224
SUKUMALCHANGRA, DINAKARA and WILLIAMS 1966 (340) 76, 73
SUKUMALCHANTRA, and WILLIAMS 1965 (A 330) 1965
SUSSMANN 1967 (376) 82, 78
SUTINEN, CHRISTOFORIDIS, KLUGH and PRATT 1965 (A 66) 209
SWARTZ 1971 (15) 11, 8
SWEET, WYATT, FRITSCH and KINSELLA 1961 (40) 20, 14
SWINNY, SWINNY and HICKS 1965 (A 67) 209
SYNDER, LEMON and MANTEL 1965 (A 393) 228
SYZGANOV, GOLOVIN and TROITSKAYA 1971 (170) 38, 32
SZADKOWSKI, SCHULTZE, SCHALLER and LEHNERT 1969 (808) 153, 151
SZCZEKLIK, TERESIAK and KOLACZKOWSKA 1971 (A 148) 214
SZUCS and LORD 1967 (A 117) 212
SZYMCZYKIEWICZ, KUNSKI and GIELEC 1970 (580) 116, 107
TAKENOUGHI 1968 (581) 116, 109
TALAMO 1971 (A 149) 214
TALAMO, ALLEN, KAHAN and AUSTEN 1968 (102) 30, 26
TALAMO, AUSTEN and ALLEN 1972 (A 150) 214
TALAMO, BLENNERHASSET and AUSTEN 1966 (A 151) 214
TANNER 1967 (341) 76, 73
TARKOFF, KUEPPERS and MILLER 1968 (A 152) 214
TAUB 1966 (A 291) 222
TAUBERGER 1964 (A 470) 1964
TAYLOR 1963 (964) 190
TAYLOR 1969 (1041) 195
TECULESCU and RACOVEANU 1972 (A 331) 224
TERRELL and SCHMELTZ 1968 (A 471) 234

TERRIS 1968 (1128) 200
TERRY (1129) 200
TERRY 1968 (889) 186
TERRY (16) 11, 8
THE CHART (1130) 200
THE JOURNAL OF SCHOOL HEALTH (1003) 192
THE JOURNAL OF SCHOOL HEALTH (1131) 200
THE LANCET 1969 (945) 189
THE LANCET 1970 (946) 189
THE LANCET 1972 (1132) 200
THE MEDICAL JOURNAL OF AUSTRALIA 1964 (947) 189
THE MEDICAL JOURNAL OF AUSTRALIA 1970 (1133) 200
THE MEDICAL JOURNAL OF AUSTRALIA 1971 (890) 186
THE MEDICAL OFFICER 1969 (965) 190
THOMSON and PAVIA 1973 (730) 138, 131
THOMSON 1970 (A 9) 205
THURLBECK (A 292) 222
THURLBECK 1963 (171) 38, 31
THURLBECK 1963 (41) 20, 17
THURLBECK 1966 (A 30) 207
THURLBECK 1970 (A 31) 207
THURLBECK 1970 (A 32) 207
THURLBECK 1971 (A 332) 224
THURLBECK and ANGUS 1963 (A 293) 222
THURLBECK and ANGUS 1964 (196) 45, 42
THURLBECK and ANGUS 1967 (197) 45, 41
THURLBECK, ANGUS and PARE 1963 (199) 45, 42
THURLBECK, BATES, FRASER and HENDERSON 1968 (A 68) 209
THURLBECK, FRASER and BATES 1965 (198) 45, 41
THURLBECK, HENDERSON, FRASER and BATES 1970 (A 294) 222
TOBACCO REPORTER 1967 (1043) 195
TOBACCO REPORTER 1967 (1042) 195
TOKUHATA, DESSAUER, PENDERGRASS, HARTMAN, DIGON and MILLER 1970, (442) 96, 88
TOKUHATA 1972 (A 221) 218
TOLL 1964 (A 69) 209
TOMASHEFSKI and PRATT 1967 (A 10) 205
TOWNLEY, RYNING, LYNCH and BRODY 1970 (A 153) 214
TRINQUET and MEYER 1971 (A 185) 216
TSUMETOSHI, SHIMIZU, TAKAHASHI, ICHINOSAWA, UEDA, NAKAYAMA, YAMAGATA and OHSHINO 1971 (582) 116, 109
TUBERCULOSIS ASSOCIATION OF MARYLAND 1968 (948) 189
TURINO 1971 (A 154) 214
TURNER 1969 (A 295) 222
TYSINGER 1970 (A 333) 224
ULMER 1970 (583) 116, 106
ULMER 1972 (A 118) 212
ULMER and REIF 1966 (586) 117, 106
ULMER, REICHEL and WERNER 1968 (585) 117, 106
ULMER and REICHEL 1970 (584) 117, 106
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE 1964 (17) 11, 8
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE 1965 (823) 160, 169
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE 1967 (18) 11, 8
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE 1967 (891) 186
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE 1968 (19) 11, 8
U.S. DEPARTMENT OF HEALTH EDUCATION AND WELFARE 1969 (20) 12, 8
U.S. DEPARTMENT OF HEALTH EDUCATION AND WELFARE 1971 (21) 12, 8
U.S. DEPARTMENT OF HEALTH EDUCATION AND WELFARE 1973 (22) 12, 8
U.S. MEDICINE 1960 (1134) 200
U.S. MEDICINE 1968 (966) 190
U.S. MEDICINE 1968 (1028) 194
U.S. MEDICINE 1969 (893) 186
VALIC and ZUSKIN 1972 (587) 117, 108
VALENTIN and WOITOWITZ 1967 (A 296) 222
VAN DER WAL, HUIZINGA, ORIE, SLUITER and DE VRIES 1966 (A 222) 218
VAN GANSE, DEPOORTER, MEHEUS, EYLENBOSCH, VANHOORNEEN, VUYLSTEEK, DE VREEZE and RAVEEL 1972 (764) 144, 141
VARGHA 1969 (A 334) 224
VARPELA and SARIS 1971 (A 155) 214
VASSAR, CULLING and SAUNDERS 1960 (229) 51, 49
VIDAL, CAZAL, ROBINET-LEVY and MICHEL 1971 (A 156) 214
VIGY 1970 (588) 117, 106
VIIKERI, JAASKELAINEN and TAHTI 1968 (A 430) 231
VINCENT 1967 (892) 186
VISWANATHAN 1965 (778) 147, 145
VISWANATHAN, MODY, PRASAD and SINHA 1965 (377) 83, 78
VOISIN 1970 (A 297) 222
VON OETTINGEN 1941 (172) 39, 33
VOORST VADER 1965 (894) 186
VOTCHAT, LOZINSKY, GRIBOVA, TAGAI and SHEFER 1970 (663) 130

VUGA 1968 (A 509) 237
VYSKOCIL 1968 (589) 117, 108
WADDELL 1966 (1004) 192
WAKERLIN 1964 (821) 160, 167
WALKER, ARCHIBALD and ATTFIELD 1971 (490) 103, 100
WALKER 1917 (A 389) 228
WALKER and KIEFER 1966 (731) 138, 134
WALLNER 1963 (23) 12, 8
WALLER 1971 (A 259) 220
WALSHE and HAYES 1967 (590) 117, 110
WATERMAN, DOMM, ROGERS and BORRELL 1969 (A 119) 212
WARE 1964 (895) 186
WARING 1969 (1135) 200
WARTHEN 1964 (1159) 202
WEBB, COCK, LANIUS and SHAW 1967 (809) 153, 150
WEBSTER, KETTEL, MORAN, BUGAIESKI and CUGELL 1968 (103) 30, 24
WEHRLE, BRENT, DOYLE, FARR, FAGAN, FINBERG, NAHMIAS, PICKERING and YAMAZAKI 1969 (A 390) 228
WEIR and DUNN 1970 (305) 68, 65
WEISS 1967 (378) 83, 79
WEISS 1968 (896) 186
WEISS 1968 (732) 138, 134
WEISS 1969 (379) 83, 79
WEISS 1971 (380) 83, 79
WEISS, BOUCOT, COOPER and CARNAHAN 1963 (616) 124, 121
WEISS and DULFANO 1968 (765) 144, 142
WEISSBECKER, CREAMER and CARPENTER 1971 (733) 138, 133
WEISSBECKER, CARPENTER, LUCHSINGER and OSDENE 1969 (283) 62, 58
WELCH, REINECKE, HAMMARSTEN and GUENTER 1969 (A 157) 214
WELLER 1955 (200) 45, 42
WENDOHL and FACKLER 1968 (949) 189
WENDEL 1966 (591) 117, 106
WENDEL 1968 (216) 48, 46
WESCHESTER MEDICAL BULLETIN 1969 (1136) 200
WESSEL-ASS 1967 (A 298) 222
WEST, GLAZIER, HUGHES and MALONEY 1969 (A 510) 237
WEST, BURNS, DANIEL and JACKSON 1959 (A 391) 228
WESTERMARK 1961 (A 472) 234
WHATLEY 1967 (826) 160, 173
WIGHTMAN 1968 (766) 144, 142
WIKLANDER and NORLIN 1957 (767) 144, 142
WILHELMSEN 1967 (664) 130, 125
WILHELMSEN, ORHA and TIBBLIN 1969 (592) 117, 105
WILHELMSEN and TIBBLIN 1966 (593) 117, 105
WILKELSTEIN, KANTOR, DAVIS, MANERI and MOSHER 1967 (342) 76, 73
WILLIAMS and ANDERSON 1968a (768) 144, 141
WILLIAMS and ANDERSON 1968b (769) 144, 141
WILSON, MEADOR, JAY and HIGGINS 1960 (617) 124, 122
WINKELSTEIN and KANTOR 1969 (240) 54, 52
WINKELSTEIN and FRENCH 1970 (A 260) 220
WINKENWERDER, ALLAN and FISHER 1962 (381) 83, 79
WOOLCOCK, BLACKBURN, FREEMAN, ZYLSTRA and SPRING 1970 (594) 117, 109
WOOLCOCK, VINCENT and MACKLEM 1969 (665) 130, 125
WOOLF and SUERO 1971 (618) 124, 121
WOLFF, PURDOM and ISENHOWER 1954 (A 457) 223
WORLD HEALTH ORGANIZATION 1970 (1137) 200
WORTH, MUYSERS and SMIDT 1968 (A 33) 207
WRIGHT 1965 (A 70) 209
WRIGHT and KLEINERMAN 1963 (A 11) 205
WRIGHT 1968 (A 34) 207
WYATT and FISCHER 1964 (A 35) 207
WYNDER, GOODMAN and HOFFMANN 165 (734) 138, 134, 133
WYNDER, GOODMAN and HOFFMANN 1965 (735) 139, 134
WYNDER and HOFFMANN 1970 (A 223) 218
WYNDER and HOFFMANN 1972 (897) 186
WYNDER, KAISER, GOODMAN and HOFFMANN 1963 (736) 139, 134
WYNDER, KAUFMAN and LESSER 1967 (619) 124, 122
WYNDER, LEMON and MANTEL 1965 (A 392) 228
WYNDER, TAGUCHI, BADEN and HOFFMANN 1968 (284) 62, 60
YAMANAKA 1970 (42) 20, 17
YANDA 1965 (A 120) 212
YANDA and MOTLEY 1965 (A 121) 212
YEAGER 1969 (285) 63, 58
ZAGONA 1967 (1138) 200
ZASLY, BAUM and RUMBALL 1960 (A 394) 228
ZEIDBERG, HORTON and LANDAU 1967 (343) 76, 73
ZEIDBERG, PRINDLE and LANDAU 1964 (443) 96, 90
ZIVY 1970 (382) 83, 79
ZIVY and FOURNIER 1970 (383) 83, 79
ZWI, GOLDMAN and LEVIN 1964 (620) 124, 121
ZWI, SLUIS-CREMER and DU PREEZ 1967 (595) 117, 108